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THE SURGICAL TREATMENT OF SOME LESIONS OF THE LOWER ESOPHAGUS AND UPPER STOMACH

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CANCERS of the lower esophagus and the cardiac end and fundus of the stomach, or both, have until recently defied attempts at curative therapy. It is true that total gastrectomy with esophagojejunostomy through the abdominal approach has been advocated during the past several years and quite a few patients have been salvaged. But abdominal resection in growths that have extended up the esophagus is impossible. And furthermore, it is impossible to determine anything about supradiaphragmatic metastases, which may occur, through an abdominal approach. Therefore, many surgeons have performed either gastrostomy or jejunostomy for feeding purposes and have not attempted radical resections. The inevitable end was postponed a few weeks or months at best. The average duration of life following such procedures is six to ten months. Rarely the patient lives for more than one year. Fortunately the outlook for these patients has become less gloomy in the light of renewed interest in the transthoracic approach to these lesions. Approximately fifty-six patients, exclusive of the present report, have been operated upon through the thorax with the performance of an esophagogastrostomy, and of these twenty-six have died, giving a mortality of 46.4 per cent. Four transthoracic gastrectomies with esophagojejunostomy have been reported with two deaths, or a 50 per cent mortality. Most of these patients were operated upon too recently for significant follow-up studies to have been reported.

The operation is based on experimental work that was done on dogs and cadavers by Biondie,[1] Gosset,[2] Mikulicz,[3] and Sauerbruch[4] between 1895 and 1905. Wendel[5] apparently attempted the first resection and anastomosis by the Murphy button technique in 1907, but the patient died of hemorrhage. Adams and Phemister[6] accomplished the first successful operation of this type for carcinoma of the lower esophagus

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in 1938. The patient was still alive at the time of the last report in 1943. Ochsner and DeBakey[7] did the first successful resection and anastomosis for carcinoma of the fundus. Garlock,[8] Churchill and Sweet,[9] and Phemister[10] have reported the largest series of operations of this type.

There are differences of opinion as to the best way to administer the anesthetic agent, perform the operation, and care for the patient postoperatively. As with other operations this is healthy and every claim probably has merit, and only by collecting and evaluating results can the proper solution be reached.

Fig. 1.—Roentgenologic barium study of a 60-year-old, deaf, mute moron with carcinoma of the lower end of the esophagus. This patient died of inanition before any surgery was attempted. On the x-ray films the growth appeared to extend up the esophagus for a distance of 8 cm. above the level of the diaphragm.

It is highly desirable that the type of lesion be indicated. This is not always done in the reports. From the literature and from limited personal experience it appears that carcinoma of the lower esophagus is more frequently operable than is carcinoma of the cardia or fundus, and the operation can be more easily done because less of the stomach and gastrohepatic and gastrocolic omenta will need removal than is the case with carcinoma of the cardia or fundus.

It has been stated that a positive biopsy must be secured before the operation is undertaken and, of course, is highly desirable in all types of surgery. On the other hand, small lesions in certain localities at the cardia are not readily accessible to the esophagoscope, gastroscope, or fluoroscope. A valuable aid in such instances is the occurrence of spasm of the lower esophagus which does not resemble the smooth coning seen in true idiopathic cardiospasm. Furthermore, the filling defect seen under the fluoroscope is not a true picture of the extent of the growth. The lesion may appear inoperable or questionably operable, and actually be a relatively small carcinoma with extensive spasm (Figs. 1 and 2). Ochsner and DeBakey[7] raised the question of exploring these patients in the absence of a positive biopsy and that suggestion should be followed. Otherwise early lesions may be postponed beyond the opportune time, or the hope of resection and esophagogastric anastomosis abandoned when actually it could be done easily. Certainly all surgeons have for years considered lesions elsewhere in the gastrointestinal tract in that light, and there is no logical reason to consider those in the lower esophagus and upper stomach in any other.

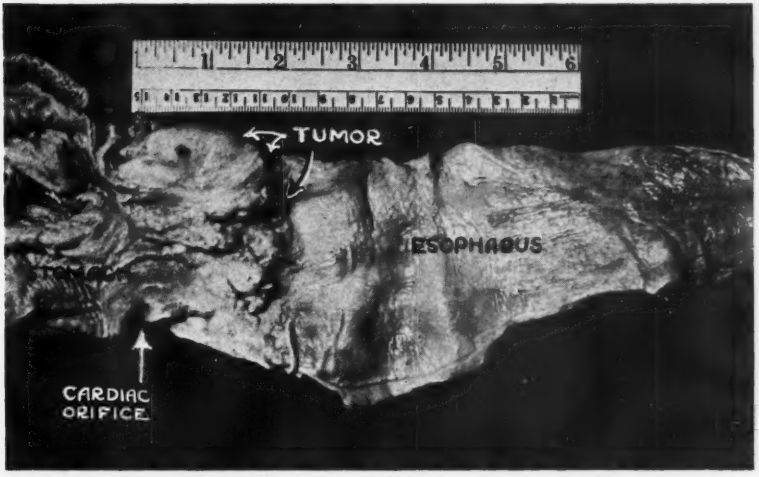

Fig. 2.—Autopsy specimen from patient whose x-ray film is shown in Fig. 1. In the fresh specimen this tumor extended only 4 cm. above the cardiac orifice. There was no submucosal extension of the tumor, there were no metastases, and this tumor was operable. These comparative measurements of the extent of the tumor on the x-ray films, and gross anatomic specimens, suggest that the extent of the lesion, judged from the x-ray films, may be considerably greater than the extent of the lesion found at operation.

There is no question but that the operation can be done under general anesthesia in the absence of an endotracheal tube. There is not the need for aspiration from the bronchial tree of pus, blood, and secretions that there is in many operations upon the lungs, nor will the stomach be distended from pressure administered through the ordinary face mask because the esophagus may be occluded during the greater part of the operation. However, if both pleural cavities are opened, which is common, it seems advisable to be in absolute control of the situation by having an endotracheal tube in place. The exact degree of inflation and deflation of the lungs can be controlled more easily. The danger of laryngeal spasm from too light an anesthetic

state is nonexistent. Many authors speak of the danger of trauma by the endotracheal tube. Experience with several hundred operations done with patients under endotracheal anesthesia does not bear out the fear of trauma.

As to the surgical approach to these lesions there is much debate. Many feel that an abdominal approach should be done to determine the presence of extension or metastases, and also to free the stomach from its attachments prior to the thoracic part of the operation. Metastases sometimes occur above the diaphragm and are not visualized by preoperative roentgen studies. Of course, the abdominal approach offers no possible means for direct visualization or palpation of such metastases. On the other hand, after the diaphragm has been incised through the thoracic approach, not only is the left supradiaphragmatic region accessible, but also the liver and other peritoneal organs can be visualized and palpated. It is easy to don the obstetrician's version glove and palpate the pelvic viscera and cul-de-sac. Of course, biopsy of suspicious areas in these regions is very difficult, if not impossible. No one would argue that the inspection can be as thorough as it is through an abdominal incision, but it appears to be quite adequate for practical purposes. If the lesion proves to be inoperable the operative insult is very little, if any more, pronounced with the thoracic than with the abdominal approach. There seems to be no logical reason for dividing the operation into stages as advocated by some, because the lesion can be completely removed and the anastomosis completed at one operation and without fear of peripheral circulatory failure in most instances. An occasional patient will have to have his nutritional state improved by means other than intravenous blood and plasma alone. Practically everyone is in agreement now that jejunostomy is preferable to gastrostomy when resection is contemplated. Jejunostomy interferes very little, if at all, with mobilization of the stomach.

At the completion of the operation it is debatable whether or not the pleura should be drained. Wu and Loucks[11] question the advisability of it, whereas most other surgeons state that they drain the pleura from three to seven days. It is only by accumulating evidence on the incidence of empyema that the answer can be reached. It is of more than academic interest because the occurrence of empyema may cause death of the patient or at least greatly prolong his hospitalization, and if neglected make it necessary to resect ribs. By the use of penicillin irrigations, the hazards of this complication may be greatly reduced. At least experience with this drug in empyema from other causes lends support to this belief. One patient in the present report did not have the thorax drained and at post-mortem twenty-four days later a small undrained empyema pocket was found, which certainly had contributed to the patient's cause of death. (The suture line between the esophagus and stomach was completely healed and intact.) When exploration is done and the condition found inoperable it is usually unnecessary to drain the thorax. Needle aspirations may, however, be required from time to time during the postoperative period.

Anyone dealing with visceral cancers is often confronted not with the possibility of a cure, but rather with the probability of palliation. There

is no place in surgery where the decision is harder to make than in dealing with these lesions. The operation is of such magnitude that it should not be undertaken lightly. And after the operation is under way, there is little opportunity to withdraw and "stage" the operation. However, the miserable end from slow starvation and pulmonary complications is so common and well known that one is justified in taking long chances in an effort to provide a relatively normal means for food intake and the disposition of oral secretions. Since it has been shown repeatedly that the esophagogastric or jejunal suture will heal with a minimal degree of stenosis in most instances, the operation should be done even if the hope for a cure cannot be entertained.

CASE REPORTS

During the last two and one-half years five patients have been operated upon by the transthoracic route and a partial or total gastrectomy performed with an esophagogastric or esophagojejunal anastomosis.

CASE 1.—L. M., a man, aged 52 years, had difficulty in swallowing for fifteen months prior to admission. Regurgitation of all solid food for two months and gastrostomy with retrograde esophageal dilatation was done elsewhere two months before entrance to the North Carolina Baptist Hospital. There had been a gradual weight loss of forty pounds over the fifteen months. The roentgenologist reported that there was an obstructive lesion at the esophageal gastric junction. The esophagus was moderately dilated proximal to the point of obstruction, and he believed the patient had more than simple cardiospasm. Biopsy taken through the esophagoscope showed no malignancy. At operation a tumor was found involving the stomach just below the esophagogastric junction. Nodes were palpable in the gastrohepatic and gastrocolic omenta. A subtotal gastric resection with esophagojejunal anastomosis was done, and an intercostal tube was placed in the thorax. The pathologist reported adenocarcinoma of the stomach. The patient recovered and left the hospital on a liberal diet including minced meats.

CASE 2.—M. S., a 71-year-old woman, ten years before admission had a large gastric hemorrhage. Since then until admission she had atypical ulcer symptoms, some nausea, vomiting, and no relief from taking food or alkali. Two weeks before entrance she had another gastric hemorrhage. She had lost thirty pounds in weight. The roentgenologist reported that there was an hourglass deformity of the stomach in the upper one-third with an irregular filling defect on the greater curvature. The gastric findings were those of carcinoma. At operation many nodes were palpable in the gastrohepatic omentum. The stomach could not be freed from the pancreas until the esophagus and pylorus had been severed and retracted forward. A segment of the body of the pancreas was removed along with the stomach. An esophagojejunostomy was done and an intercostal tube placed in the thorax. The pathologist reported no evidence of malignancy, but a 3 cm. ulcer. The patient recovered.

CASE 3.—P. H., a man, 58 years of age, had substernal discomfort and regurgitation of most of his food intake for nine months prior to admission. He had lost thirty pounds in weight. The roentgenologist

reported that the esophagus was normal. There was an extensive filling defect in the mid-portion of the stomach extending well up on the lesser curvature and posterior gastric wall. The findings were those of extensive carcinoma of the stomach. A gastroscopic examination showed a firm obstruction at the cardia of the stomach. At operation a large mass was palpable in the mid-portion of the posterior gastric wall and along the lesser curvature up to the cardia. Total gastrectomy with esophagojejunostomy and intercostal tube drainage was done. The pathologist reported adenocarcinoma of the stomach. The patient died seven days after operation because of leakage from the duodenal stump. The esophagojejunal anastomosis was intact and well on the way to complete healing.

CASE 4.—C. P., a 32-year-old man, had four years of symptoms suggestive of duodenal ulceration, three months of melena, and one month of regurgitation of food before admission. His weight loss had been thirty-seven pounds. The duodenal cap showed a tender spastic deformity and a demonstrable ulcer crater. The findings were those of carcinoma of the lower third of the esophagus and an active duodenal ulcer. A biopsy taken through the esophagoscope showed adenocarcinoma. At operation a hard mass was found extending from the stomach up into the lower 2 cm. of the esophagus. A partial gastric resection with esophagogastrostomy and intercostal tube drainage was done. The pathologist reported adenocarcinoma of the esophageal cardiac junction. The patient recovered.

CASE 5.—S. A., a woman, aged 54 years, had no complaints other than progressive difficulty in swallowing and thirty-two pounds weight loss over a period of one year prior to admission. The roentgenologist reported that the esophagus showed moderate dilatation with a point of obstruction at the cardiac orifice, with a slight irregular filling defect on the left lateral wall of the esophagus. The diagnosis was either cardiospasm or neoplasm. An esophagoscopy showed cardiospasm only. At operation a mass was found in the fundus of the stomach which was densely adherent to the spleen and pancreas. A subtotal gastrectomy, splenectomy, and removal of the tail of the pancreas were necessary. This was done, followed by esophagogastrostomy without intercostal tube drainage. The patient died on the twenty-fourth postoperative day from empyema on the left side, subphrenic abscess of the left side, and bronchopneumonia. The anastomosis was completely healed and smooth. The pathologist's report on the specimen was anaplastic carcinoma of the cardia and fundus of the stomach. Areas of mucinous carcinoma were present.

DISCUSSION

The present series of cases is small, but if all such cases are reported it should help to clarify the proper surgical approach to lesions which have heretofore been considered practically hopeless. There are three transthoracic esophagojejunostomies, and two transthoracic esophagogastrostomies. Only four other esophagojejunostomies by the thoracic route have been reported. Undoubtedly others have been done and not reported or the reports have been unintentionally overlooked. It seems to

be the procedure of choice if the lesion extends into the esophagus and if there are palpable nodes in the gastric omenta. It has certain advantages over total gastrectomy by the abdominal route. The suggestion of Churchill and Sweet[9] about lengthening the mesentery of the jejunal loop seems a good one. It was not necessary in these three cases. The question of enteroenterostomy is debatable. The patient who died from leakage of the duodenal stump might have been saved by an enteroenterostomy which should have prevented duodenal distention. On the other hand, the other two patients recovered satisfactorily without enteroenterostomy. It seems more likely that the duodenum was not properly closed. The patient who died following esophagogastrostomy, among other complications, developed an empyema of the left thorax. This could have been prevented by intercostal tube drainage. The two deaths can be attributed to some extent, at least, to errors that can be corrected. It is interesting to note that in none of the living patients was there evidence of constriction at the point of anastomosis at the time of discharge from the hospital, and in the patients who died, the anastomosis was well healed, or in the process of healing without leaks or narrowing. A prolonged follow-up will determine the occurrence of late constriction. Certainly a few months of life during which solid foods and liquids can be taken in a relatively normal way are superior to life with a gastrostomy tube.

These cases are presented to help to establish the feasibility of the operation. The final status and utility of the operation will depend upon the experience of many surgeons during the next few years. It is recognized that a high incidence of cure is not to be expected as yet. However, some cures will be obtained. Even in those patients not cured the remaining portion of their lives can be made more tolerable than if they lead a gastrostomy existence. Rather than condemning these patients by a hopeless prognosis based on fluoroscopic and esophagoscopic findings alone, it is hoped that more of these patients will be given the benefit of a transthoracic exploration.

SUMMARY

1. Some lesions of the lower esophagus or the cardiac end and fundus of the stomach, or both, have until recently defied attempts at curative therapy.

2. Approximately fifty-six patients with cancer of this region have been operated upon, to date, through the thorax. Four patients had total gastrectomies and esophagojejunal anastomoses. The other patients had subtotal or partial gastrectomies with esophagogastric anastomoses.

3. The operative mortality is 46.6 per cent. The follow-up period has been too short, in most instances, to be significant.

4. Three patients with esophagojejunostomies and two patients with esophagogastrostomies are reported in the present series. One of the latter had ulcer and not cancer.

5. It is emphasized that spasm, as seen under the fluoroscope, is frequently out of proportion to the size of the lesion. In fact spasm may be the only positive finding which, along with the clinical story, warrants surgical exploration.

6. The transthoracic and transdiaphragmatic approach, with the patient under endotracheal anesthesia, is quite satisfactory.

7. The operation should be done as a palliative measure in some instances even if all hope of a definite cure has been abandoned.

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READHESION AFTER INTRAPLEURAL CAUTERIZATION

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LOSS of effective pulmonary collapse through early readhesion of the lung to the parietes is an infrequent but serious complication of closed pneumonolysis. It is widely regarded as an irremediable condition, inevitably entailing the abandonment of pneumothorax therapy. The object of this article is to discuss briefly the causation and prevention of the complication, and to give an account of the endoscopy findings and results in six cases in which an operative attempt to reestablish an efficacious collapse was undertaken.

CLASSIFICATION

Obliteration of a pneumothorax space after adhesion section may occur in three forms:

1. *The Acute Obliteration.*—The acute obliteration usually develops within forty-eight hours of operation, and is often total. It is generally considered a sequel to lung re-expansion as a result of massive escape of air from the pleural cavity, in the presence of pleural changes that lead to rapid adherence of the visceral and parietal surfaces. Pulmonary emphysema, severe postoperative coughing or vomiting, and inadequate closure of trocar puncture sites are regarded as the

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chief causes of the lung re-expansion. Recently, Brantigan, Hoffman, and Proctor[1] have described cases which suggest that endobronchial tuberculosis may be a factor, by producing, after pneumonolysis, a check valve type of bronchial obstruction that results in rapid re-expansion of the lung and loss of pneumothorax space.

2. *The Secondary Obliteration.*—Secondary obliteration occurs within a week or two of operation and tends to be more localized than the first variety, the sites of predilection being the posterior mediastinum, the paravertebral gutter, and the area of posterior chest wall between the rib angles and posterior axillary line referred to endoscopically as the scapular zone. Divided adhesion surfaces, alone or in conjunction with previously intact pleural surfaces, may be involved. Faulty post-operative posture, inadequate control of intrapleural pressures, or a combination of both are the important causal factors.

3. *The Late Obliteration.*—Late obliteration is nearly always a sequel to postoperative effusion. It is outside the scope of this paper.

PATHOLOGY

Exposure to the gases of a pneumothorax gradually alters the lining pleural surfaces. They eventually become covered with a fine pellicle of organized lymph, and tend to adhere readily when allowed to come into contact. However, at the stage when pneumonolysis is usually performed—that is, in the early months of pneumothorax—these changes are, as a rule, absent or little marked, and the pleural layers do not necessarily become adherent when allowed to touch for a few hours or even days. Gowar's[2] experiments on artificial pleurodesis illustrate well the difficulty of producing adhesions in a relatively normal pleura. But after section, additional factors predisposing to obliteration are present, namely, raw exuding cauterized surfaces, particularly projecting adhesion stumps; traumatic pleuritis; and small amounts of blood in the pleural cavity, from chest punctures or adhesions.

Derscheid and Toussaint,[3] discussing the formation and evolution of intrapleural adhesions, point out that when any deposit of fibrin, lymph, or blood occurs on the pleura, the coagulum is progressively invaded by connective tissue elements, which may subsequently persist or disappear. These authors believe that the vascular recent adhesions, composed of young cellular connective tissue, rich in capillaries, spring from an actively inflamed visceral pleura. They suggest that, after division, adhesions of this type are more likely to readhere than the older, standing whitish structures, composed of dense avascular fibrotic tissue, that arise from a visceral pleura which is no longer actively inflamed.

LITERATURE

Coulaud[4] described one case of acute obliteration with complete re-expansion of the diseased lobe, occurring forty-eight hours after incomplete section in a patient with bilateral pneumothorax. Brissaud[5] mentioned two cases developing within twenty-four and forty-eight hours of operation. Bilateral disease was present in both, and cough was severe. This author suggested that raising of the parietal pleura by subpleural emphysema might be a contributory causal factor.

Moore[6] reported one case of his own and six cases collected from the literature. These include the three cases already referred to, two cases described by Jacobaeus, and one by Forsee. Douady and Meyer[7] observed two cases of localized obliteration, in which, after extensive cauterization, the large raw surfaces had readhered within twenty-four hours of operation and could not be detached by refills. Mistal[8] encountered one acute obliteration. Alexander[9] reported one case of complete loss of collapse after total adhesion section, as a consequence of surgical emphysema.

More active measures were adopted in two cases of localized re-adhesion described by Zimmermann.[10] In one patient, there had been some hemorrhage during detachment of a long stiff adhesion from the posterior apical region. Three days afterward, the initial screen examination showed the stalk, projecting from a well-collapsed lung, adherent at about the sixth rib in the scapular zone. Thoracoscopy was again carried out immediately on this patient. The end of the adhesion was attached to the posterior cannula puncture site. After an attempt at blunt separation failed, it was enucleated. In a second case, where scapular membranes had been divided, lateral obliteration was noted four days later. Thoracoscopy on the seventh day showed the lung widely adherent to the original cauterization area in the scapular region. This readhesion was too short for division; an attempt at blunt separation was made but discontinued on account of hemorrhage, and thoracoplasty eventually had to be performed. There was no marked surgical emphysema or generalized lung re-expansion in either case, and in both posture seems to have played an important part in producing the readhesion.

Michetti[11] reported a case of acute obliteration in a patient with bilateral pneumothorax. The more recently collapsed lung had almost entirely re-expanded within sixteen hours of a total pneumonolysis, following vomiting and severe coughing with resultant massive subcutaneous emphysema. At operation slight bleeding had occurred and a subacute inflammation of the visceral pleura had been noted; a large effusion in the costophrenic sinus followed. An air pocket was found and refills were pushed for some days, with re-establishment of the pneumothorax anteriorly and laterally, but by the fourth day it was evident that the lung was widely adherent to the posterior chest wall. Thoracoscopy was then repeated on the patient; the greater part of the symphysis was easily detached with the cold cautery blade; a few denser adhesions required section. A complete remobilization of the lung was achieved and maintained without complication.

Four patients were encountered by Brantigan, Hoffmann, and Proctor[1] in whom closed pneumonolysis was followed by rapid re-expansion and loss of pneumothorax space. Fluoroscopic examinations were performed three hours after completion of the pneumonolysis, and re-expansion was by then almost complete. Marked subcutaneous emphysema was present. Refills were given immediately and repeated within four hours. The following morning complete re-expansion had occurred in one case; in the other three cases the upper and middle lobes had expanded, but there was a partial collapse of the lower lobe.

In all four cases, bronchoscopy subsequently revealed endobronchial lesions at the orifices of the branch bronchi, which had caused partial obstruction.

INCIDENCE

Lung re-expansion with readhesion occurred in six, or 0.29 per cent, of the 2,043 cases of pneumonolysis collected by Moore.[6] It is only fair to point out that the great majority of cases are never recorded, that minor degrees of readhesion are never noticed and, in consequence, these figures make the condition seem much rarer than it really is. Seven authors reporting the complication mention the number of operations performed. In their series, the incidence of readhesion is 1.3 per cent of the total number of pneumonolysis operations (Table I). This figure gives a truer indication of the frequency of the grosser forms of the complication.

TABLE I

INCIDENCE OF LUNG READHESION

AUTHOR	OPERATIONS	OBLITERATIONS
Alexander	137	1
Brissaud	50	2
Coulaud	139	1
Forsee	26	1
Jacobaeus	150	2
Mistal	50	1
Zimmermann	200	2
Total	752	10 (1.3 per cent)

Seven instances of secondary or localized readhesion have been encountered by the writer in a series of 459 pneumonolysis operations, an incidence of 1.5 per cent. There were no cases of acute obliteration. Radiographic review of the series revealed seven additional patients in whom minor degrees of readhesion, unimportant clinically because of their situation, length, or tenuity, had developed. The total incidence of readhesion was 3.0 per cent.

PREVENTION

Maintenance of Collapse.—Excessive escape of air from the pleural cavity can nearly always be avoided by employment of premedication that reduces to a minimum the vomiting which tends to follow any intrapleural cauterization (in my own experience, omnopon and scopolamine produce the least aggravation in this respect), avoidance of prolonged operative sittings, careful massage, closure and compression of cannula puncture wounds, and sedation of cough after operation.

Some degree of surgical emphysema usually develops but, with adequate radiologic supervision and attention to refills, permanent deterioration of pulmonary collapse rarely results. The importance of keeping the pneumothorax lung well down for some weeks after adhesion section is generally recognized; it not only lessens the risk of contact between lung and chest wall, but, after total cauterization, by eliminating tension on the lung stumps and permitting their full retraction until cicatrization has occurred, may reduce the incidence of postoperative effusion.

Fluoroscopy.—The importance of strict fluoroscopic control of collapse during the immediate postoperative period can hardly be overemphasized. The ideal routine is that recommended by Alexander.[12] The patient is screened daily until fresh surgical emphysema has ceased to develop; in most cases, leakage of air stops within two or three days of operation. After that, fluoroscopy is performed twice weekly for the next fortnight. If this procedure were followed in every case and refills given as indicated, the incidence of obliteration would be kept at the lowest possible level and readhesion, if it did occur, would be detected at the early fibrinous stage, when operative reseparation presents least difficulty.

Posture.—Less often stressed is the importance of nursing posture after pneumonolysis. If attention is not paid to posture, readhesion of divided stumps to the parietes or localized fusion between uncauterized visceral and parietal surfaces may occur, even when the lung is well collapsed.

Patients should not be left to their own devices because they tend to lie on the unoperated side, flat on the back, or in the semisupine position, the last two being particularly dangerous. Most thoracoscopists recognize this and prescribe posture to a certain extent, nursing their patients sitting up after an apical cauterization, or lying on the unoperated side following division of lateral adhesions. The term "lateral" is used here in its thoracoscopic sense, to denote an adhesion inserted below the second rib. In point of fact, the insertions of the majority of these are posterolateral or posterior and a lateral posture does not prevent contact between long posterolateral stalks and the parietes, however well the lung is collapsed. This fact is frequently demonstrable at the final endoscopic survey after cauterization, when, with the patient in a true lateral position on the operating table, the ends of stumps detached from the scapular region may be seen lying in contact with the paravertebral gutter or vertebral bodies. Liability to readhesion and the need for careful posturing are probably greatest after incomplete division, when the adhesions which remain may prevent wide separation of near-by stumps from the chest wall.

Although the liability to secondary readhesion varies greatly from case to case and, provided an adequate collapse be maintained, is admittedly small after the complete division of a few nonrigid adhesions, it is advisable to posture every patient for at least ten days after cauterization. This should be extended to two weeks or longer when there is gross alteration of the visceral or parietal pleura, after an extensive cauterization, when the affected lobe is heavily infiltrated and bulky, where stiff projecting stumps are slow in merging into the general lung contour, after incomplete section, or when cauterization is followed by considerable effusion in the costophrenic sinus.

When all the severed adhesions spring from the same lung zone, the choice of position is straightforward. For apical adhesions, the best posture is upright; for axillary adhesions, lying on the unoperated side, flat or with the body elevated; for posterior or posterolateral adhesions, lying in an oblique position on the unoperated side with the body rotated forward forty-five degrees, or sitting up and leaning

slightly forward; for anterior and anterolateral adhesions, sitting upright; and for mediastinal adhesions, sitting up slightly inclined toward the operated side.

After cauterization of multiple adhesions arising from different aspects of a lung or lobe, the most useful compromise position is adopted, for example, for the frequent combination of adhesions from the apical and posterolateral upper lobe segments, the patient is postured sitting upright and leaning slightly forward, or lying on the unoperated side rotated forward with the shoulders well elevated. Patients do not find these postures irksome, particularly when several alternatives can be given, and cooperate willingly. The supine and semi-Fowler positions are at all times strictly forbidden. Some variant of the sitting up position should always be employed if postoperative effusion is more than minimal.

DIAGNOSIS

While the possibility of readhesion should be borne in mind when, following pneumonolysis, considerable surgical emphysema develops, or the intrapleural pressures rise steeply after a small refill, the diagnosis is essentially fluoroscopic. The total or subtotal obliterations will, of course, be obvious. The lesser degrees, too, since they are always posterior, are easily discovered by fluoroscopy. The lung becomes fixed to that part of the thorax wall where there is least respiratory movement. The resulting relative immobility of the adherent zone immediately strikes the observer. If a stump alone is involved, the previously mobile projection no longer moves up and down or from side to side with respiration or cough; as the patient is rotated behind the screen the tip of the stalk moves with the posterior arc of the rib to which it is attached. When the visceral and parietal pleurae around the stump are involved in the obliteration, no adhesion projection may be visible beyond the lung contour, but a considerable area of lung is seen to have lost most of its respiratory mobility and to move only with the posterior costal segments.

TREATMENT

In my view, the treatment of established readhesion should be operative, the only contraindications being an extensive tuberculosis of the pleura or a pneumothorax in which the collapse achieved by the original pneumonolysis is inadequate and not susceptible of improvement by a subsequent stage.

An unsuccessful attempt to break down the obliteration by refills is recorded in most of the cases in the literature. Theoretically, if instituted sufficiently early, it should be feasible, and one sees from time to time pressure changes during pneumothorax insufflation which suggest that pleural separation is occurring, but whether of surfaces gummed together by fibrin or merely by capillary attraction is uncertain. So, while the method may be given a trial, it should not be persisted in if not immediately effective. The readherent areas may be too short or extensive for further cauterization or even enucleation, and only separable by blunt dissection. It is important that operation should be undertaken early while blunt separation is still possible.

Six cases of readhesion have been treated by reoperation, five immediately when the condition was discovered and the sixth, in which the diagnosis was made late, seven weeks after the original cauterization.

At rethoracoscopy a small effusion was found in every case. The adhesion was in the posterior half of the hemithorax, involving the posterior mediastinum, vertebral bodies, paravertebral gutter, and often the scapular zone as far out as the posterior axillary line. There was usually direct adhesion between visceral and parietal pleurae in addition to readhesion of stumps. More rarely, there were long, slender newly formed bands or sheets, presumably sequelae of temporary contact between uncauterized pleural layers coated with blood or lymph.

When the patient was reoperated on early, it was possible to separate the readherent stumps by blunt dissection; later they had to be cauterized. The outer layer of the readhesion was invariably the densest part. All the visceroparietal obliterations separated bluntly. The earliest phase of readhesion appeared to be a fibrinous gluing together of the opposing surfaces; at this period, blunt separation was easy and relatively avascular. At a later stage, when the adhesion was composed of granulation tissue, blunt detachment was still practicable, but accompanied by considerable parietal oozing. This either ceased spontaneously or could be checked quickly by application of the cautery. In the third stage there was formed fibrous tissue, dense and inseparable by gauze dissection when a cauterized area was involved, but usually fine, areolar, and easily broken down, when previously intact pleural surfaces were affected.

In no case could the duration of readhesion before operation be estimated within narrow limits but, taking the shorter possible period in each as representing the age of the attachment, the readherent cauterized surfaces were separable by blunt dissection within two or three days of attachment and the direct visceroparietal fusions after a considerably longer period.

The lung was remobilized and the pneumothorax continued without complication in four cases. Tuberculous empyema followed in one case with multiple tubercles on the visceral pleura. Persistent effusion developed in another where the collapse after the original pneumonolysis was inadequate.

CASE REPORTS

CASE 1.—Mr. D. G., aged 23 years, a motor engineer, was admitted to King George V Sanatorium, Godalming, in February, 1938, with a four months' history of cough and expectoration. X-rays showed a left upper lobe tuberculosis with multiple infraclavicular cavitation. The sputum contained tubercle bacilli. A left artificial pneumothorax was induced, Feb. 28, 1938.

May 4, 1938, incomplete pneumonolysis was done. A few pleuritic bullosa blebs were seen on the parietal pleura and on the adhesions. There were some inoperable paravertebral sails. Numerous lateral adhesions, including a membrane four inches wide arising from an obliterated interlobar fissure, were divided.

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No special posture for nursing care was adopted. There was little surgical emphysema. An effusion reaching the top of the diaphragmatic cupola developed, and on the fifth day, 250 c.c. of blood-stained fluid was aspirated. Refill pressures rose rather steeply but nothing unusual was noticed at the routine biweekly fluoroscopy until twelve days after operation, when the pneumothorax lung was seen to be readherent in the mid-zone as far out as the axilla. A film taken two days later confirmed the screen findings.

May 18, 1938, fourteen days after section, the patient was thoracoscoped again. The lung was directly adherent to the chest wall in the paravertebral region from the third rib to the diaphragm. A buttress formed by readherence of the fissural membrane ran laterally from the paravertebral fusion out to the axilla. This was separated with the cold cautery point. The soft granulation tissue fixing the adhesion scar to the chest wall gave way easily for the most part, only one denser strand requiring cauterization. Separation was carried almost to the edge of the main paravertebral symphysis. Freeing of the latter was not attempted, as the risk of perforating the lung was deemed too great. It was hoped that removal of the lateral buttress had produced sufficient relaxation to permit cavity closure. There was considerable oozing from the granulation tissue bed but this stopped soon after separation. Some coagulated blood was removed with the aspirator.

Nursing care was administered with the patient in the right lateral position. There was no febrile reaction and no effusion. Subsequent films showed the lung margin well medial to the axilla and displaying no tendency to creep outward. Expectoration ceased ten weeks after reoperation and within four months cavitation was no longer visible.

COMMENT

In this case, posterolateral adhesion took place between the ninth and twelfth days after operation. It would seem to have resulted from a combination of incomplete section, slight hemorrhage, effusion, and incorrect posture, rather than surgical emphysema. At the time of reoperation, the adhesion was between three and five days old. One dense strand required division; the remainder was detachable by blunt dissection. Nothing was known at the time of any previous application of this procedure, its results, or possible complications, and it was therefore restricted to a zone where the lung surface was protected by a layer of old adhesion, no attempt being made to break down areas of direct symphysis between lung and chest wall. In the light of further experience it seems probable that the paravertebral fusion could have been separated safely by gauze dissection.

CASE 2.—Mr. H. U., aged 34 years, a clerk, was admitted to the Surrey County Sanatorium, Milford, in October, 1940. He had been in a sanatorium in 1934 and a right phrenic avulsion had been performed at that time. After discharge, he remained well and worked for five years. In March, 1940, he began to cough, expectorate, and lose weight. On admission he was subfebrile and expectorating two ounces of positive sputum daily. X-rays showed a raised right diaphragm with multiple discrete calcified foci in the lower half of the lung field. The left

lung was emphysematous; there was a large thin-walled cavity in the upper zone and discrete mottling of a mixed type in the middle and lower zones. A left artificial pneumothorax was induced in November, 1940 (Fig. 1).

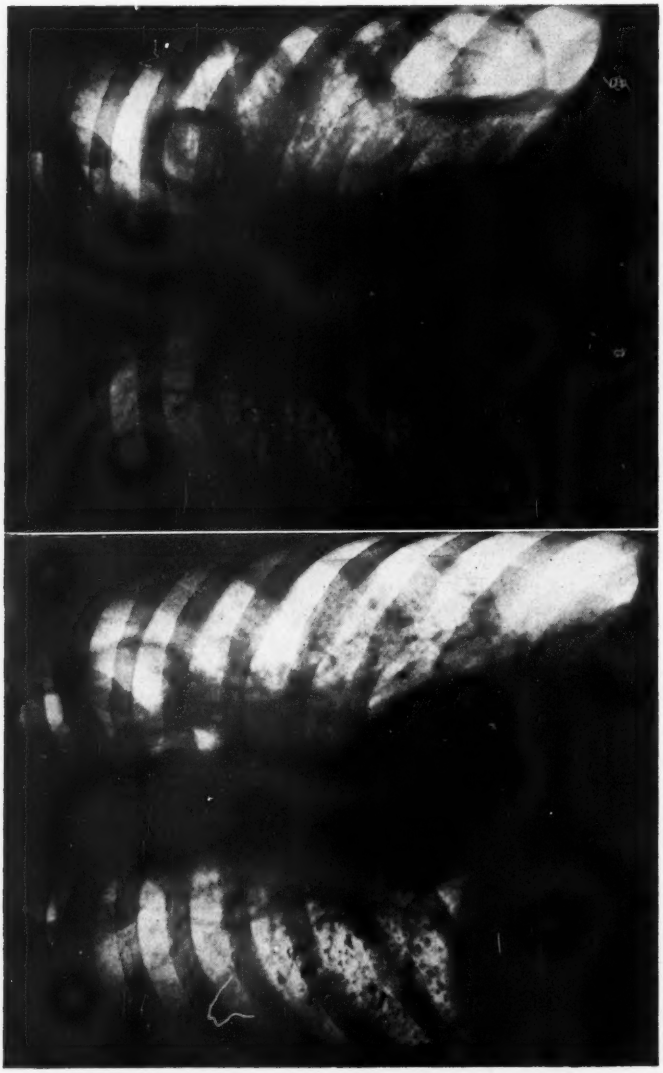


Fig. 1.

Fig. 2.

Figs. 1 to 4.—Case 2. Man, aged 34 years. Onset, 1934. Right phrenic avulsion, 1934. March, 1940, sputum positive and cavitation of left upper zone. Nov. 16, 1940, left artificial pneumothorax. Jan. 16, 1941, total adhesion of section. Jan. 29, 1941, remobilization of adherent pneumothorax lung.

Fig. 1.—Radiograph, Dec. 9, 1940. Raised right diaphragm. Multiple calcification of lower half of lung field. Left artificial pneumothorax. Adhesions over large upper zone cavity.

Fig. 2.—Radiograph, Jan. 18, 1941, twelve days after pneumonolysis. Surgical emphysema of pectoralis major. Cut stump adherent to sixth rib. Posterior surface of lung adherent below this. Vertical band of opacity marks outer border of fusion in lower third.

Jan. 16, 1941, there was complete adhesion of the section. A stout triangular system was disinserted from the upper three ribs in the scapular and paravertebral zones. A band to the head of the first rib was divided. Fluoroscopy immediately afterward showed the lung free and well collapsed.

No special posture was adopted for nursing care. There was no increase in the small sinus effusion present before operation. Surgical

emphysema was moderate. Refills were given on the day following section and again on the fifth day. Some time after the second refill a large pectoral collection of emphysema appeared during a bout of coughing. This was not reported and nothing was noticed amiss until the emphysema was discovered on the twelfth day at a refill during

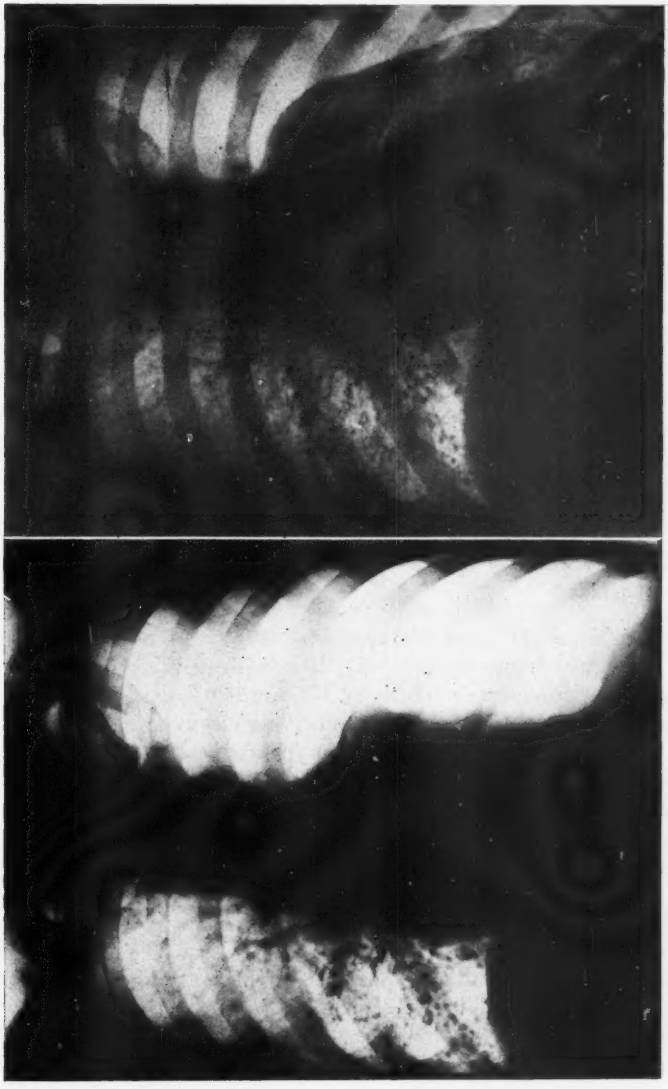


Fig. 3.

Fig. 4.

Fig. 3.—Radiograph, March 27, 1941. Complete remobilization.
Fig. 4.—Radiograph, Oct. 10, 1941, nine months afterward. Selective collapse being developed. Pneumothorax dry.

which the intrapleural pressures were found to rise more rapidly than usual. Fluoroscopy showed partial re-expansion of the pneumothorax lung; the cavitated upper lobe was fixed and immobile on respiration (Fig. 2).

Jan. 29, 1941, thirteen days after section, thoracoscopy was done and blunt dissection of the newly formed posterior adhesion. The stump

of the larger adhesion, recognizable by its yellowish-white end scar, had readhered to the sixth rib in the inner scapular zone. Below and medial to this, there was a complete fusion between lung and posterior chest wall, down to the diaphragm and in to the mediastinum.

With a gauze pledget, mounted on a Heaf forceps, blunt separation was begun at the adhesion stump. Once a line of cleavage had been established by firm swab pressure, the interior of the readhesion stripped easily. After the stump had been freed, separation of the direct visceroparietal fusion was accomplished without difficulty, the fine areolar tissue that formed it parting under gentle pressure with only moderate oozing. The lung was completely freed in to the vertebral column and down to the diaphragm (Fig. 3).

The postoperative reaction was minimal. The sinus effusion did not increase and was soon absorbed. The patient was given nursing care lying on his face or inclined forward on the right side. Refills were pushed for some weeks. Three months after the second intervention the cavity was no longer demonstrable and tubercle bacilli had disappeared from the sputum (Fig. 4).

COMMENT

Readherence occurred between the fifth and twelfth days after cauterization. The exciting cause, late escape of air from the pleural cavity, was predisposed to by pulmonary emphysema. The adhesion, operated on when, at most, one week old, was readily detached by gauze dissection. It consisted of (a) readhesion of a lung stump, and (b) a direct visceroparietal fusion. Of these, the latter was the more easily separable.

CASE 3.—Mr. A. D., aged 24 years, linotype operator, was admitted to Milford Sanatorium in October, 1941, with an eighteen months' history of cough and expectoration. He was febrile and in poor general condition. There was one ounce of positive sputum daily. X-rays showed bilateral disease with cavitation in the right upper and dorsal lobes and in the left lingula. A right artificial pneumothorax was induced Aug. 5, 1942.

Sept. 23, 1942, the section was incomplete. No fluid was seen. A massive short adhesion, two inches in diameter, running from the dorsal segment of the lower lobe to be inserted from the fifth to the seventh interspaces in the costovertebral gutter, was detached from the chest wall. A stout pillar from the posterior surface of the upper lobe to the third rib and interspace was divided. A higher adhesion system was left for a further stage (Fig. 5).

There was no febrile reaction. A small sinus effusion developed. Surgical emphysema was moderate. No special posture was adopted.

Oct. 22, 1942, four weeks later, there was a second stage, incomplete adhesion section. A little fluid was present. The posterior surface of the lower lobe, in the neighborhood of the adhesion divided at the first stage, was directly adherent to the chest wall below the seventh rib, from the mediastinum out to the scapular zone. Separation was not attempted.

A stout upper lobe membrane was stripped from the upper three ribs in the axillary and scapular zones. It was then seen that the

upper lobe still remained adherent by a narrow and inoperable lung-mediastinal fusion behind the innominate artery.

The febrile reaction lasted five days. There was no increase in the pre-existing sinus effusion. The patient was postured for a fortnight either on the left side, well rotated forward, or sitting upright and leaning forward. The large projecting adhesion stump was freely mobile at fluoroscopy eleven days after section, but at the next examination, one week later and a few days after posture treatment had been abandoned, it no longer moved up and down, or from side to side, with deep respiration or cough. On rotating the patient, the stump and the posterior arc of the fifth rib moved together; it appeared to be stuck to this rib one inch lateral to the transverse process (Fig. 6).

Sept. 9, 1942, eighteen days after section, thoracoscopy and blunt separation of the reformed adhesion were done. One fibrin thread hung loose from the costal pleura. Anteriorly, part of the cut surface of the stump was free; it was covered by a smooth layer of old clot. The posterior third of this surface was readherent to the fourth and fifth ribs near the outer border of the paravertebral gutter. This readhesion formed the lateral apex of a triangle, over which the posteromedial surface of the upper lobe was directly adherent to the costovertebral gutter, vertebral bodies, and posterior mediastinum. By gentle swab pressure, the lung was stripped, without difficulty, into the line of the rib heads and down to the upper edge of the older standing lower lobe fusion (Fig. 7). There was considerable capillary oozing from the raw surfaces after separation. This ceased spontaneously.

Nursing care was given with the patient on the unoperated side, rotated forward, and refills were given every second day to average end pressures of zero with the object of keeping the lung well down. There was no febrile reaction until the seventh day, when the temperature rose sharply and remained up for some weeks with the development of a moderate-sized effusion containing tubercle bacilli (Fig. 8). This patient died a year later of bronchopneumonia following a large hemoptysis from the left lingular cavity. The effusion on the right side had persisted, but remained clear, and although further reexpansion of the lung had occurred as a result of obliterative pleurisy, both the upper and dorsal lobe cavities were apparently closed. Permission for necropsy was not obtained.

COMMENT

Readhesion developed after each stage in this case. Following the first cauterization, cut dorsal lobe adhesions and a wide area of surrounding lung adhered to the posterior chest wall. This was discovered at thoracoscopy one month later; it should, however, have been detectable by careful fluoroscopy. On the preoperative film it was obscured by the lung markings of a bulky lower lobe. Later, when this lobe was less expanded, the typical obliteration edge, clear-cut medially, fading away laterally, was unmistakable (Fig. 8). This direct fusion was not divisible and, as it was probably one month old and firmly organized, blunt separation was not attempted.

After the second stage, a divided adhesion and the posterior surface of the lobe medial to it became adherent. Although no bleeding was

observed during section, some ooze occurred from the lung end of the adhesion afterward; it was only on this stump that blood clot was found at rethoracoscopy. Readhesion took place late, sometime between the eleventh and eighteenth days, and probably after postural

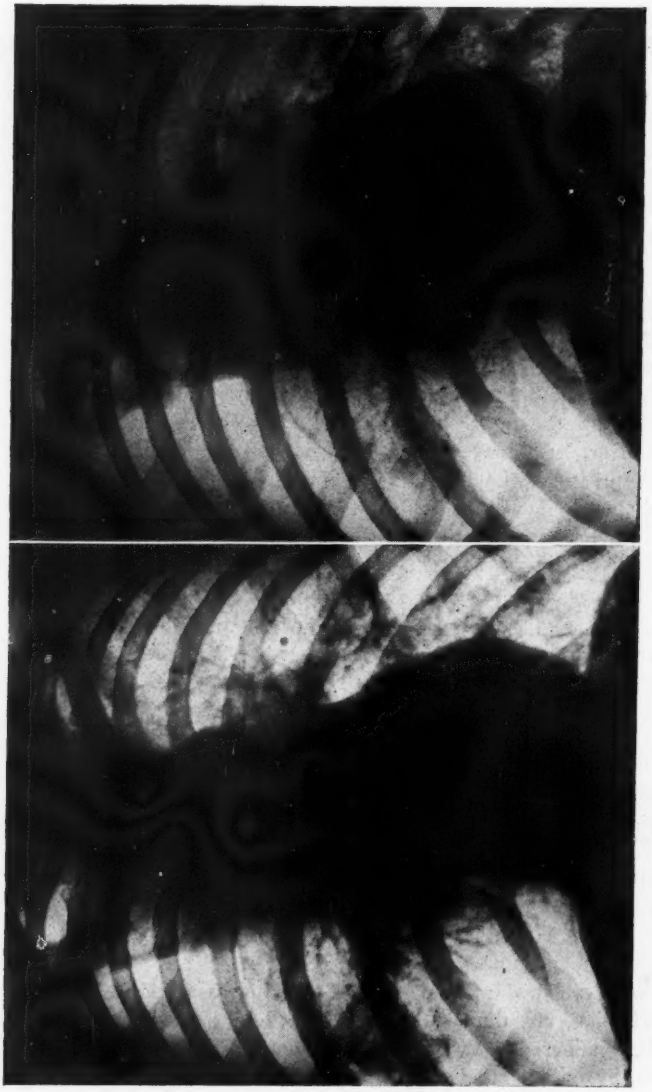


Fig. 5.

Fig. 6

Figs. 5 to 8.—Case 3. Man, aged 24 years. Onset, 1940. Aug. 5, 1942, right artificial pneumothorax. Sept. 23, 1942, incomplete pneumonolysis. Posterior readhesion followed, but was not detected until second stage pneumonolysis, Oct. 22, 1942, and was then inoperable. Nov. 9, 1942, mobilization of fresh readhesion.

Fig. 5.—Radiograph, Oct. 9, 1942. Cavity in left mid-zone. Right artificial pneumothorax with upper zone cavity suspended by lateral and mediastinal adhesions. Extensive lower lobe readhesion present is not detectable on this film.

Fig. 6.—Radiograph, Nov. 9, 1942, eighteen days after section. Adhesion stump readherent to fifth rib.

treatment was discontinued on the fourteenth day. It was easily separated by blunt dissection within four days of its formation. One fibrin thread attached to the parietal pleura represented a failed attempt at readhesion.

Reseparation was followed by persistent effusion. The delay in appearance of fever and exudate until the seventh day suggests that

this was due to overfilling an incomplete pneumothorax with an undivided adhesion composed entirely of lung tissue, rather than to the reseparation intervention, which was easy and nontraumatizing.

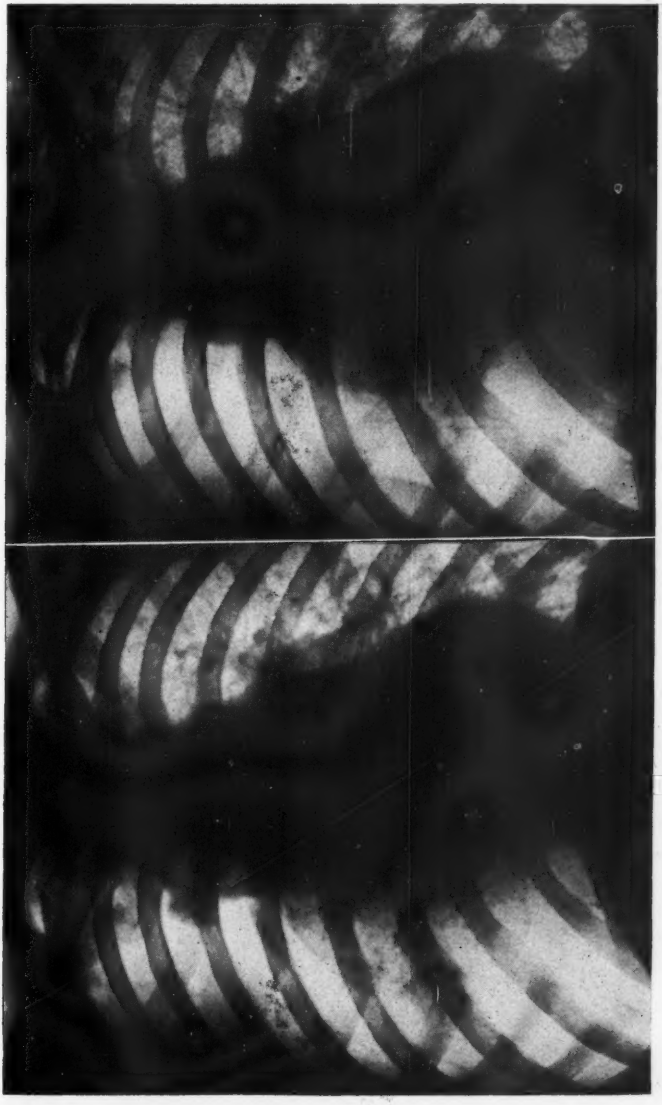


Fig. 7.

Fig. 8.

Fig. 7.—Radiograph, Nov. 9, 1942, immediately after remobilization. Stump lies more medially and an interspace lower. Fluoroscopically it again moved freely with respiration.

Fig. 8.—Radiograph, Nov. 20, 1942, eleven days later. Stump has moved further downward and medially. Cavity not visible. Edge of lower lobe fusion, no longer obscured by lung markings, is seen running downward below seventh rib. Sinus effusion present.

CASE 4.—Miss M. C., aged 20 years, a shop assistant, was admitted to Milford Sanatorium in September, 1942, with a seven months' history of cough, expectoration, and hemoptysis. She was febrile and producing two ounces of positive sputum daily. X-rays showed abundant mottling throughout the left lung field and a large cavity in the upper zone. A left artificial pneumothorax was induced, Oct. 13, 1942 (Fig. 9).

Nov. 11, 1942, there was complete adhesion of the section. A trace of fluid was present; no tubercles were seen. Several bands and membranes to the subclavian vessels and upper three ribs were divided.

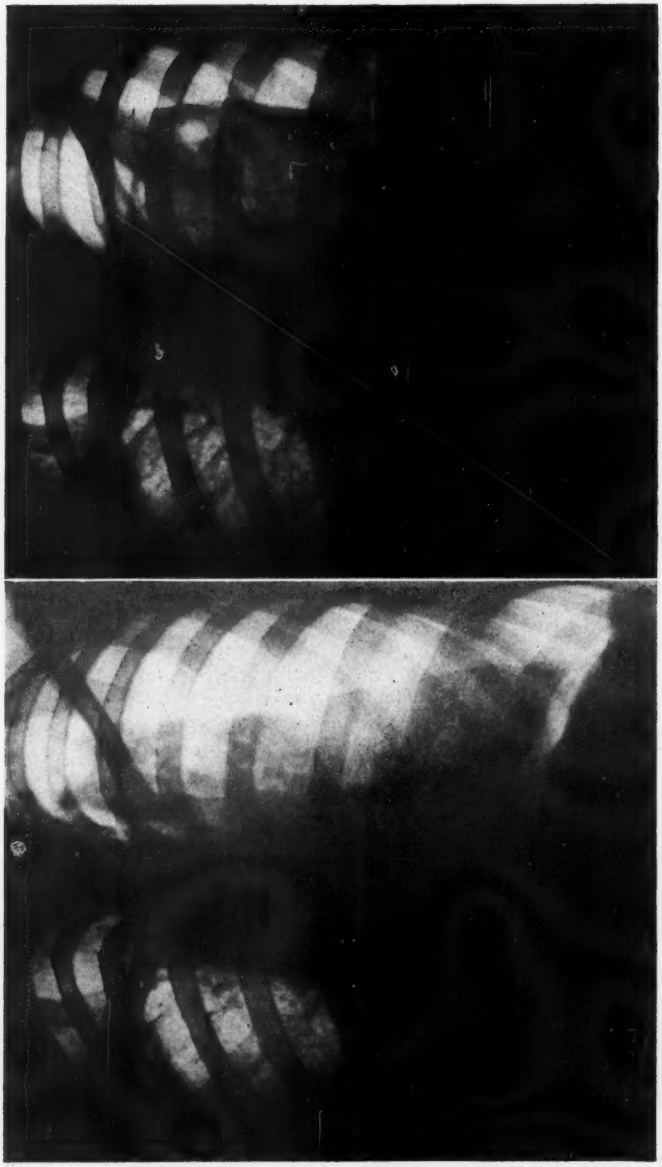


Fig. 9.

Fig. 10.

Figs. 9 to 12.—Case 4. Woman, aged 20 years. Onset, 1942. Oct. 13, 1942, left artificial pneumothorax. Nov. 11, 1942, total pneumonolysis. Nov. 24, 1942, remobilization of adherent lung.

Fig. 9.—Radiograph, Nov. 3, 1942. Left artificial pneumothorax. Cavitated upper lobe suspended by adhesions.

Fig. 10.—Radiograph, Nov. 24, 1942, thirteen days after total cauterization. Stump readherent to third rib and lung widely adherent in paravertebral gutter.

The intervention was followed by a stiff febrile reaction lasting nine days, and fluoroscopic control was deferred until this had subsided. The patient was allowed to lie back on a bedrest much of the time. Refills were followed by a sharp exacerbation of fever, but there was nothing unusual in the amounts or pressures. Surgical emphysema was not

excessive. The first fluoroscopy, on the thirteenth day, showed wide readherence of the pneumothorax lung posteriorly below the level of the clavicle. There was an effusion reaching the dome of the diaphragm (Fig. 10).

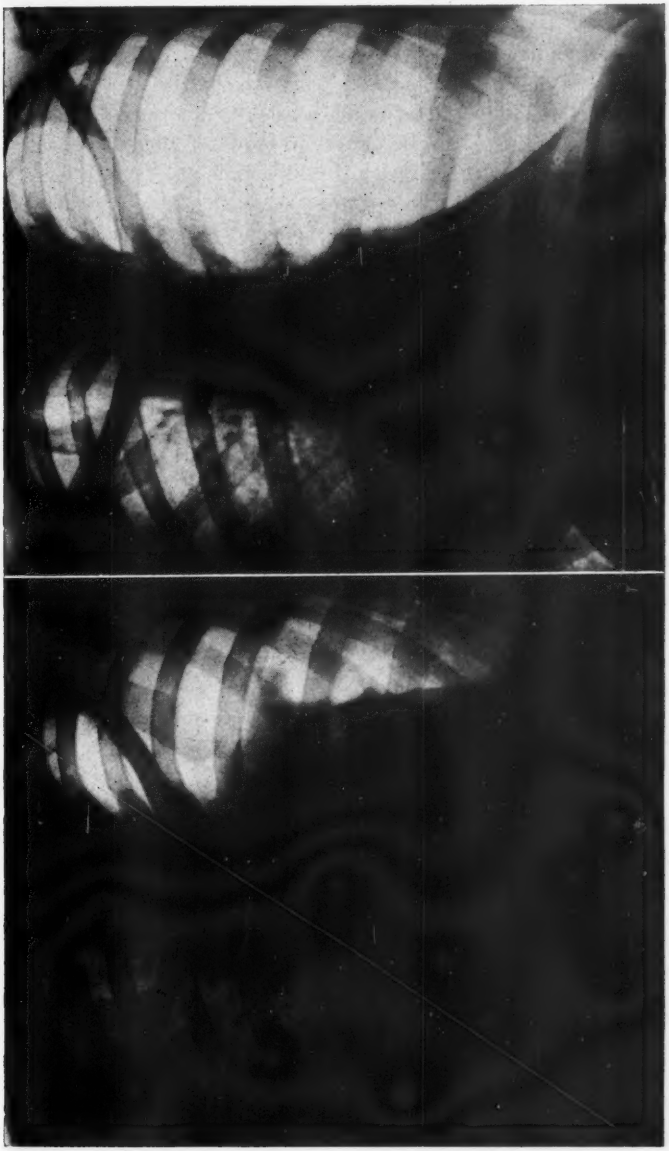


Fig. 11.

Fig. 12.

Fig. 11.—Radiograph, Nov. 25, 1942, immediately after complete refreeing of the lung by combined cautery enucleation and gauze dissection. The long rigid detached stump shows well. The danger of such a projection readhering despite good lung collapse, if strict attention is not paid to posture, is obvious.

Fig. 12.—Radiograph, Feb. 24, 1943, three months later. Cavity closed, pneumothorax dry.

Nov. 25, 1942, fourteen days after cauterization, reoperation was performed. There was some fluid. The splayed end of a stout conical adhesion stump had readhered widely to the third and fourth ribs in the scapular zone. It was free all around; on the upper sur-

face there was a shallow furrow between chest wall and adhesion; elsewhere, the junction appeared complete. There was nothing to distinguish the insertion surface from that of an uncauterized adhesion. Blunt separation with a mounted swab proved impossible; no line of cleavage could be found in the outer capsule. This was sectioned close against the chest wall and the interior of the base then separated bluntly with the cold cautery. Separation was difficult; there was considerable bleeding (more than an ooze) from the chest wall, and when freeing was complete, this had to be checked by cauterizing the raw area. More medially, a less dense adhesion, based around a small readherent stump, was separable by gauze dissection, the most difficult part being the capsule. Anteriorly, a well-vascularized and completely organized band, four inches long, was divided. No adhesion had previously existed here.

From the sixth rib down to the diaphragm, the lung was adherent from the scapular zone in to the mediastinum; laterally, by a tough elastic fibrin pellicle; inside this, by long loose areolar tissue; and still further medially, directly to the chest wall. The lung was freed in to the vertebral bodies; the fibrin and loose areolar layers separated easily on blunt gauze dissection and, more medially, the visceral pleura was peeled off the parietal without difficulty by the same procedure. At the end of the intervention the lung was quite free (Fig. 11).

For nursing care the patient was rolled forward on the right side for fourteen days and the lung was kept well down for some weeks. The temperature fell to normal, for the first time since admission, within six days of reoperation. There was no increase in the amount of fluid in the costophrenic sinus. Three months later, the pneumothorax space was dry, the cavity had closed, expectoration had ceased, and the patient's condition was steadily improving (Fig. 12). The subsequent course of the pneumothorax has been uncomplicated.

COMMENT

Failure to screen the patient at frequent intervals and faulty posturing were primarily responsible for the loss of pulmonary collapse in this case. Readhesion seems to have occurred early; a fortnight after operation, organization was almost complete in two adhesions, one a readherent stump, the other a newly formed band, presumably the result of transient contact between visceral and parietal pleurae.

A mild preoperative pleuritis was temporarily exacerbated by cauterization. It probably favored the formation of the extensive posterior obliteration. As in other cases, this separated much more easily than the readherent stumps. Although organized connective tissue was present, it consisted of fine areolar adhesions which were easily broken down. The lesser density of the direct visceroparietal obliterations may in part be explained by postulating a later origin, as a sequel to readhesion of stumps, but the noninvolvement of raw, fibrin-exuding surfaces is probably the important factor. Reseparation in the presence of pleurisy without demonstrable tubercles was uncomplicated.

CASE 5.—Miss A. M. S., aged 22 years, a clerk, was admitted to Milford Sanatorium in October, 1942, with a three months' history of cough and lassitude. There was a trace of sputum containing tubercle bacilli.

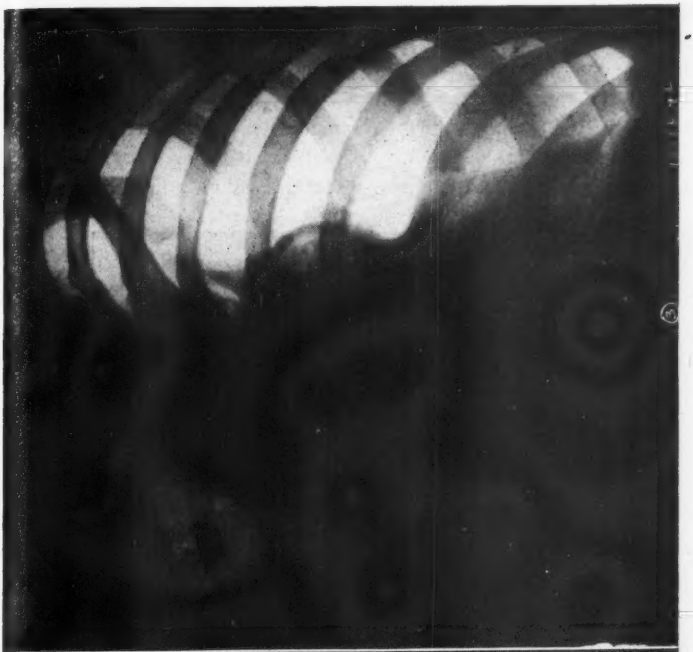


Fig. 13.

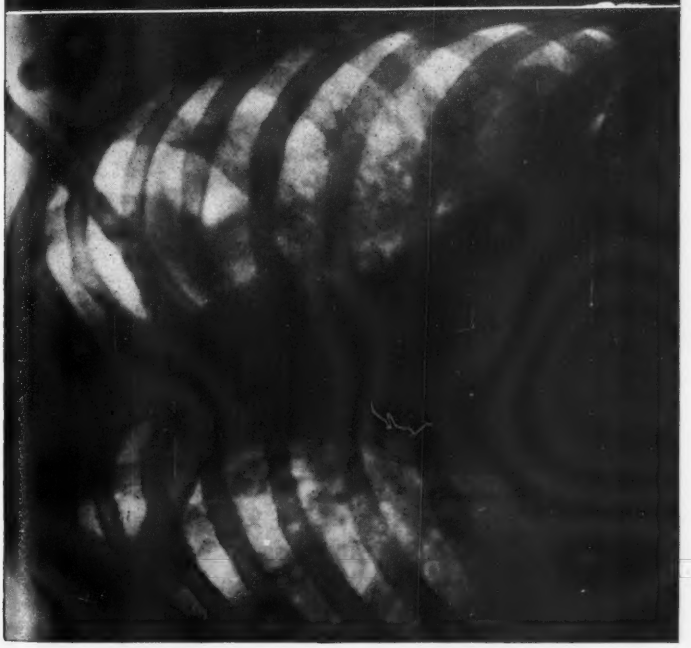


Fig. 14.

Figs. 13 to 15.—Case 5. Woman, aged 22 years. Onset, 1942. Oct. 22, 1942, left artificial pneumothorax. Dec. 3, 1942, total pneumonolysis. Jan. 21, 1943, cautery division of readhesion.
Fig. 13.—Radiograph, Nov. 17, 1942. Left artificial pneumothorax. Adhesions to large upper lobe cavity.
Fig. 14.—Radiograph, Dec. 15, 1942, twelve days after complete section. Patent cavity suspended to fifth rib by readhesion containing a long lung stalk.

X-rays showed bilateral mottling with a large cavity in the left infraclavicular zone. A left artificial pneumothorax was induced Oct. 22, 1942 (Fig. 13).

Dec. 2, 1942, there was complete adhesion of the section. There was a trace of fluid, but no tubercles, and the pleura was normal in appearance. Scapular and paravertebral membranes from the base of the upper lobe and apex of the lower, to the fourth and fifth ribs, and membranes, pillars, and bands from the upper lobe to the pleural dome and mediastinum were divided. The lung was entirely freed.

The febrile reaction was mild; there was no increase in sinus effusion and surgical emphysema was moderate. The patient was placed in the right lateral position. As early as the third day, fluoroscopy showed the cavitated upper lobe suspended by an adhesion to the

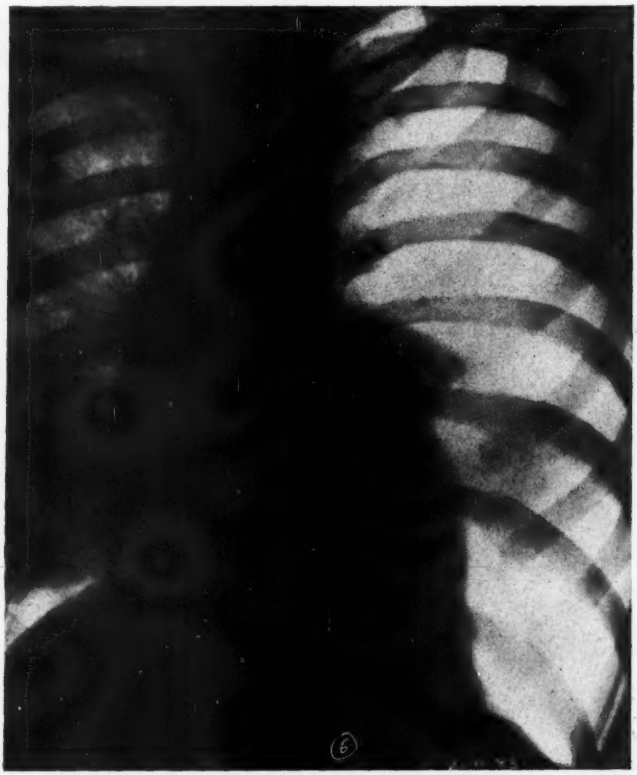


Fig. 15.—Radiograph, Feb. 2, 1943, two weeks after recauterization. Cavity closure.

posterior arc of the fifth rib. This was not recognized at the time as readhesion; it was assumed that cauterization had been incomplete. The diagnosis was made after examination of an x-ray film (Fig. 14) taken on the twelfth day, which confirmed the screen findings. Another, taken six weeks after operation, showed lengthening of the suspending sheet.

Jan. 21, 1943, seven weeks after section, thoracoscopy and cautery division of reformed adhesions were done. The base of the upper lobe and apex of the lower were attached to the costovertebral gutter, vertebral bodies, and aorta by a long U-shaped membranous adhesion, composed of arachnoid tissue, with many stouter, well-vascularized bands. It was all cauterized, with the exception of the lower end of a limb

inserted above the hilum; seizure of this with the hook cautery provoked cough, and division was terminated at the middle of the aortic arch.

The postoperative febrile reaction was mild. There was no increase in effusion. Fig. 15 shows the collapse twelve days after reoperation. Two months later, the pneumothorax was dry, the cavity had closed, and expectoration had ceased. The subsequent course of the pneumothorax has been uncomplicated.

COMMENT

The case is an example of readhesion from incorrect posturing despite maintenance of good lung collapse after operation. Readherence was a sequel to employment of the lateral position after division of mediastinal and paravertebral adhesions. It occurred within three days of operation but was not recognized while blunt detachment was still feasible. Seven weeks after formation, an extensive membrane which had lengthened in the interval was treated by cauterization. Readherent stumps were apparently the basis of this membrane, the intervening gaps being filled by long arachnoid adhesion between previously free pleural surfaces.

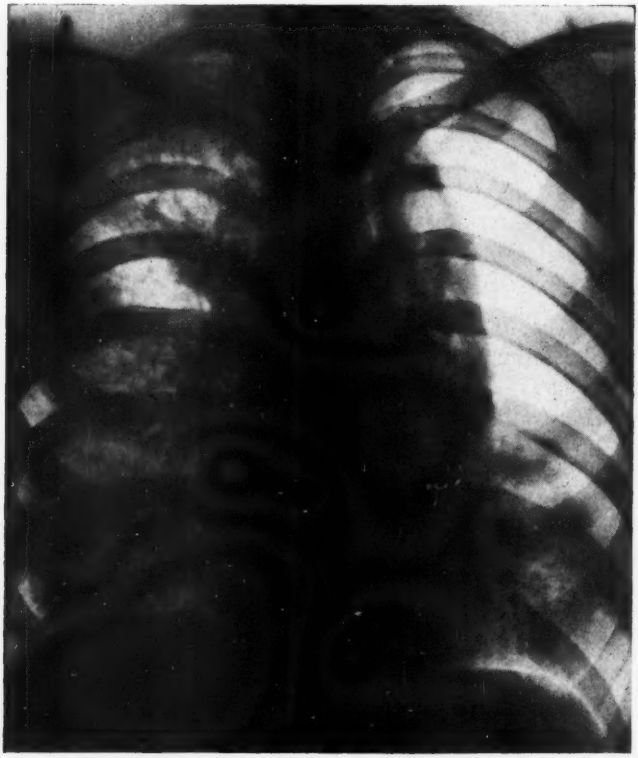
CASE 6.—Miss H. L. H., aged 18 years, a machinist, was admitted to Milford Sanatorium in December, 1942, suffering from bilateral exudative tuberculosis with multiple cavitation in the left upper lobe. She gave one year's history of cough, expectoration, and loss of weight. The evening temperature was 102.2° F. and there was one ounce of positive sputum daily. A left artificial pneumothorax was induced Jan. 11, 1943 (Fig. 16).

Feb. 18, 1943, there was partial adhesion of the section. The visceral pleura over the upper lobe was thickened, opaque, and studded with small tubercles; there were a few conglomerate subpleural tubercles. Membranes to the pleural dome, scapular and paravertebral regions were detached. Extensive mediastinal membranes were incompletely divided down to the posterior end of the aortic arch.

Although the cauterization was not total, at screening immediately afterward the lung appeared entirely free, the apex lying below the level of the aortic knob. Nursing care was administered with the patient placed on her right side. The postoperative febrile reaction lasted five days. Surgical emphysema was not severe and nothing unusual was noted in refill amounts or pressures. However, fluoroscopy on the fifth day showed the cavitated apex of the upper lobe readherent to the mediastinum above the level of the aortic arch (Fig. 17). A small sinus effusion was present.

Feb. 25, 1943, the seventh day. Rethoracoscopy and blunt separation of adhesions were done. There was a little fluid. The posteromedial part of the lung was directly adherent to the inner part of the paravertebral gutter, vertebral bodies, and mediastinum, from the third rib down to the diaphragm. The mediastinal fusion extended forward above the aortic arch for some distance in front of the subclavian artery. Except in one area, blunt separation was easy. Above, the lung was freed down to the aortic arch; posteriorly, in to the de-

scending aorta; and below, down to the diaphragm. As a swab-holding forceps was not available, a rounded diathermy electrode and the end of a second thoracoscope were used for stripping. These proved clumsy dissectors, but sufficed for this easy strip. A denser membrane to the rib heads, vertebrae, and posterior end of the aortic arch was too resistant for blunt detachment. It was apparently readhesion that had occurred early in the angle left between lung and chest wall after partial division of a membrane on to the aortic arch at the first intervention (Fig. 18).



Figs. 16 to 18.—Case 6. Woman, aged 18 years. Onset, 1941. Jan. 11, 1943, left artificial pneumothorax. Feb. 18, 1943, partial adhesion section. Feb. 26, 1943, mobilization of readherent lung.

Fig. 16.—Radiograph, Feb. 2, 1943. Left artificial pneumothorax. Cavitated upper lobe suspended by adhesions.

The immediate postoperative febrile reaction had settled by the fifth day. The temperature rose again on the twelfth day with increased effusion, which subsequently became purulent. Eighteen months later, the cavities on the left are closed and the lung is being expanded under a tuberculous pyopneumothorax. The patient is afebrile and the sputum is negative; improvement in general condition and gain in weight have been marked and continue. The disease on the right has hardened slowly and the patient is now fit to undergo left thoracoplasty for obliteration of the residual empyema space.

COMMENT

There was no gross surgical emphysema in this case. Readhesion was the result of faulty posturing, the right lateral position after division of left mediastinal and paravertebral adhesions. Detachment was accomplished bluntly without difficulty, when the adhesion was between three

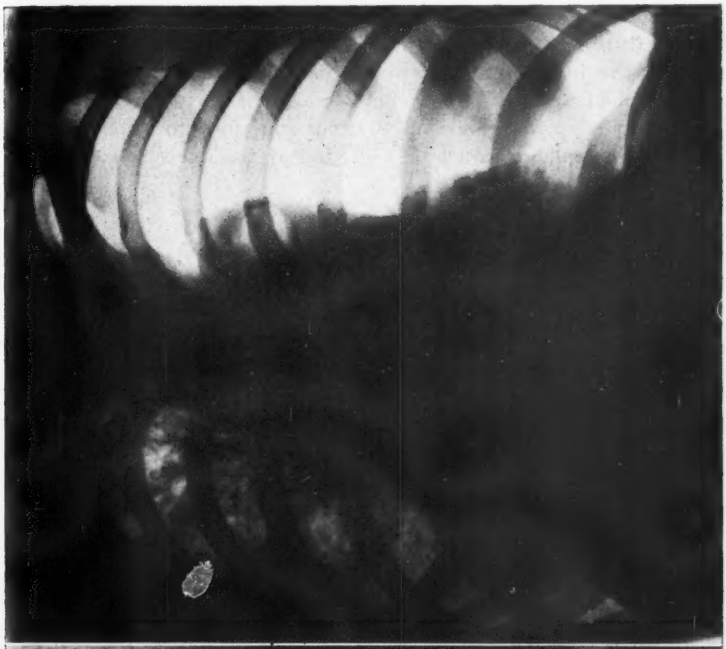


Fig. 17.

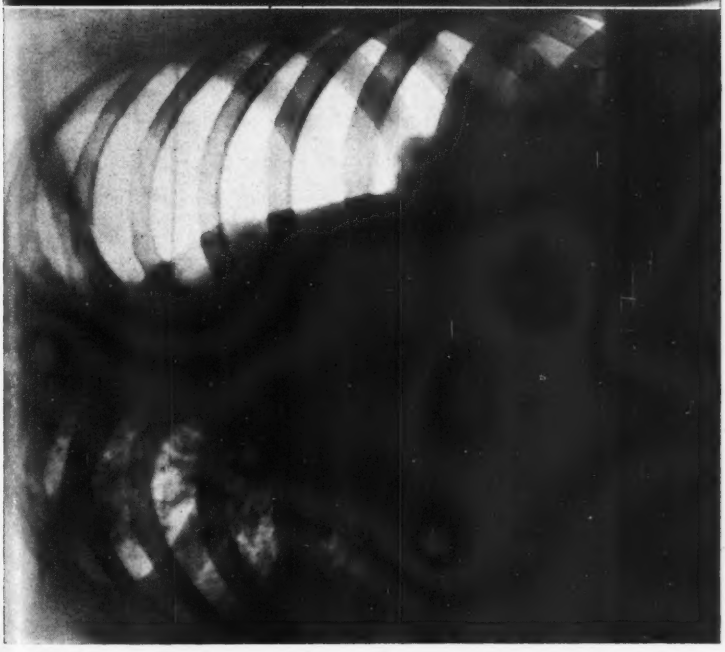


Fig. 18.

Fig. 17.—Radiograph, Feb. 24, 1943, six days after section. Lung adherent to mediastinum and paravertebral gutter.
Fig. 18.—Radiograph, Feb. 25, 1943, immediately after remobilization. Lung apex well below aortic arch.

and seven days old, except in one area, where readhesion of a partially divided membrane had presumably occurred soon after cauterization. Some readhesion possibly develops after many partial divisions, in the angle left between lung and chest wall. Its protective action may well explain why this procedure is, on the whole, less often complicated than might be expected.

Reoperation was followed by tuberculous empyema. Although the exudative nature of the disease, the multiple tubercles on the visceral pleura, and the incomplete release of the lung from adhesions all marked the pneumothorax as one particularly liable to pleural complication, the restrip intervention, entailing as it did manipulation of a tubercle-strewn pleura, must be regarded as the exciting cause of the empyema.

SUMMARY

Readhesion of the lung to the parietes after closed pneumonolysis is discussed and the literature reviewed.

Seven instances of the condition are reported. Six were treated by operative remobilization, five by immediate intervention and detachment of the lung, and one by cauterization seven weeks after readhesion.

Tuberculous empyema followed remobilization in one patient with tuberculosis of the pleura. Persistent effusion developed in another patient in whom the collapse achieved by the original pneumonolysis was unsatisfactory.

In the four patients in whom the original collapse was complete or adequate and the pleura free from tuberculous involvement, the lung was remobilized and pneumothorax continued without complication.

I am indebted to Mr. J. E. H. Roberts, Mr. N. R. Barrett, and Dr. M. L. Kohnstamm for their helpful advice and criticism of the text. I wish to thank Dr. R. J. Allison and Dr. J. Watt, Medical Superintendents of the Surrey and King George V Sanatoriums, for use of case records and radiographs.

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PRESTERNAL CYST

Report of a Case

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A REPORT of "ciliated, columnar epithelial lining" on microscopic examination of a benign subcutaneous cyst removed from the sternal region aroused interest and led to further investigation of its structure. The observations, which are unusual for a cyst in this location, are the basis of this report.

REPORT OF A CASE

Jan. 10, 1944, a woman, 55 years of age, who was of Norwegian descent, came to the Mayo Clinic because of a lump over the sternum which had been present as long as she could remember. Throughout the years this small rounded mass had remained unchanged in size and had caused no symptoms. Eighteen months before admission, however, a small white "pimple" had appeared over the center of the mass and soon afterward had begun to discharge a small amount of thin, milky fluid. The drainage had continued in amounts just sufficient to require daily dressings to prevent soilage of underclothing. No episodes of increased swelling, pain, redness, or heat had occurred to suggest acute inflammation. There had been no associated discomfort or obvious odor. The history from a medical and family standpoint was not significant.

The results of general physical examination were entirely negative except for an oval, slightly fluctuant tumor in the midline, overlying the junction of the manubrium with the body of the sternum. Its transverse diameter was about 5 cm. and its vertical diameter was slightly less. There was no discoloration or abnormality of the overlying skin. A small amount of milky fluid could be expressed through a minute opening over the center of the tumor. The results of routine laboratory studies and roentgenographic examination of the chest were negative. No abnormality of the sternum could be detected.

Excision of the cyst was advised. January 14, one of us (O. T. C.) removed a subcutaneous cyst from the front of the sternum at the level of the sternal angle. This cyst measured 5 by 4 by 4 cm. No unusual vascularity or abnormality of the sternum was noted. Because of fixation and shallowness of the subcutaneous tissues over the sternum, obliteration of the dead space created by removal of the cyst was impossible. A Penrose drain was inserted and was allowed to remain for forty-eight hours. The margins of the skin were separated subsequently to allow more adequate drainage, after which healing progressed by second intention. When the patient was dismissed from our care on the twenty-third postoperative day the incision was almost completely healed.

On macroscopic examination the cyst was unilocular, measured 5 by 4 by 4 cm., and was filled with fluid material that appeared to be pus. The wall was uniformly thin (1.5 to 2.0 mm.) and the lining was smooth and soft. The cyst was covered by a considerable amount of loosely adherent fat except on the surface next to the skin.

On microscopic examination the wall appeared to be divided into three layers (Figs. 1 and 2). The innermost layer was a mucous membrane of pseudostratified, columnar, ciliated epithelium. Immediately external to this was a thin layer of loose connective tissue containing numerous small blood vessels, many fine nerve bundles, frequent small collections of lymphocytes, a few mucous glands, and, rarely, a small piece of hyaline cartilage. Many sections were examined from six tissue blocks cut from widely separated areas of the wall of the cyst. Alternate sections were stained with hematoxylin and eosin and van Gieson's connective tissue stain. No smooth muscle fibers could be found except in the walls of numerous small blood vessels. The third and outermost layer, which comprised approximately 60 per cent of the entire thickness of the wall, was composed of rather dense collagenous bundles.

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DISCUSSION

A consideration of the nature of the tumor described in the foregoing report must be based on speculation. However, the striking similarity between its structure and that of so-called bronchogenic cysts of the mediastinum cannot fail to elicit some comment.

Adams and Thornton,[1] in 1943, gave the following description of bronchogenic cysts of the mediastinum, "Grossly the cysts are very thin-walled and are filled with a milky-colored, mucoid material containing desquamated epithelium which is under considerable pressure. They project more often toward the right side. The lining is smooth and consists of flattened to columnar ciliated epithelium. In some places there is no epithelium. The remainder of the cyst wall consists of fibrous tissue, smooth muscle, mucous glands, cartilage, nerves, and blood vessels." They suggested that since these cysts usually are situated on the right side just above the carina they conceivably might arise as small tracheal diverticula which are "pinched off" during development of the fetus.

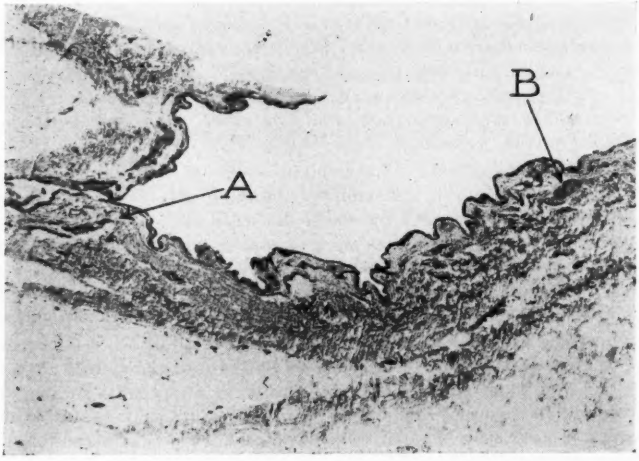

Fig. 1.—Entire thickness of wall of cyst, showing mucosal lining. *A*, A collection of mucous glands; *B*, a small piece of hyaline cartilage (×15).

Chiari[2] reported five cases of diverticulum of the trachea. The diverticula were all situated in such positions that if they were pinched off they might give rise to mediastinal cysts. No communication between the cavity of the cyst and the lumen of the trachea or major bronchi has been reported. Heuer and Andrus[3] discussed Stilling's report of a cyst of considerable size in the anterior mediastinum and stated that under these circumstances the thymus should be suspected as a source. Apparently a cyst of this character situated outside the thoracic cavity never has been reported. In the fifth week of intrauterine development, the trachea and buds of the main bronchi are apparent but complete fusion of the right and left mesenchymal bars of the sternum into a single median piece does not occur until early in the third month.[4] During the period between the appearance of the bronchial buds and fusion of the sternal bars, a mediastinal cyst, which developed from a diverticulum, conceivably could migrate into a presternal position.

Perhaps the cyst was really a teratoma. Its histologic structure and midline position can be explained on this basis. Other origins have been considered but they are not supported by the known facts in the case. For example, cysts of the thyroglossal duct[5] and laryngeal diverticula[6] are not lined with ciliated, pseudocolumnar epithelium and do not occur in this situation.

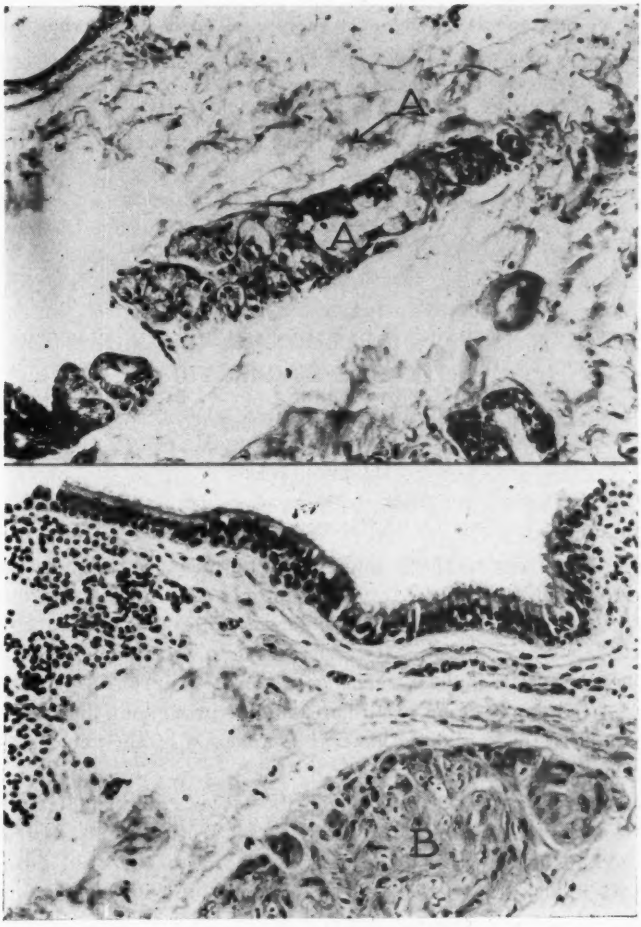

Fig. 2.—*Upper, A,* mucous glands indicated by *A* in Fig. 1; *lower, B,* small area of hyaline cartilage indicated by *B* in Fig. 1. Note pseudocolumnar, ciliated epithelium overlying cartilage and submucous lymphoid collections to its left (×200).

SUMMARY

A cyst, lined with ciliated, pseudocolumnar epithelium, which was located in the subcutaneous tissues at the sternal angle was encountered in the case of a woman 55 years of age. Its walls, which were thin, contained mucous glands, cartilage, vessels, and nerves. This cyst bore a striking similarity to bronchogenic cysts of the mediastinum. Other authors have suggested that these bronchogenic cysts arise as small tracheal diverticula which are pinched off during development of the fetus, and also that they arise from the thymus. Apparently no cyst of this description outside the thoracic cavity previously

has been reported. The most likely explanation of origin seemed to be that it was a mediastinal cyst that had migrated into a presternal position or that it was a teratoma.

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THE QUESTION OF PULMONARY DAMAGE WITH ARTIFICIAL RESPIRATION

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SO MANY different methods and machines for artificial respiration have been described during recent years that not only the layman but also the physician is in a quandary as to the relative effectiveness of each. Furthermore, the efficiency of mechanical versus manual methods has been the subject of considerable discussion.[1-5] Since "controlled respiration" during certain operative procedures is being used increasingly throughout the country, it was thought worth while to make a general comparison of the various procedures by which the lungs may be ventilated.

A clear and definite distinction exists between artificial and controlled respiration but unfortunately the majority of workers and writers use the terms interchangeably. The term *artificial respiration* should be applied to those efforts expended by an operator when spontaneous movements on the part of the subject are impossible and external methods are necessary to sustain or restore life. *Controlled respiration* results when external efforts have increased the minute respiratory volume sufficiently to reduce the tension of carbon dioxide in the blood below the concentration necessary to stimulate the respiratory center. As a result no spontaneous movements occur. The anesthetist by his efforts then can regulate the respiratory movements of the patient. Spontaneous respiration is resumed on cessation of the efforts of the operator as the normal carbon dioxide tension of the blood is restored.

Recent investigations of artificial respiration have been made with regard to circulatory effects and ventilation.[6, 7] The main purpose of this study has been to determine whether any damage was done to the lungs of laboratory

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animals by various forms of artificial respiration and to correlate the variations of pressure occurring in the application of the several methods with any morphologic changes that may have been produced.

METHODS

Dogs were used in the sixty-nine experiments in this investigation. Anesthesia was accomplished by the use of one of the following agents: nembutal, amytal, chloral hydrate and urethane, diethyl ether, cyclopropane, or avertin. After it was determined that the anesthetic agent per se was *not* a factor in producing pulmonary damage of the type under investigation, nembutal administered intravenously was used for most of the remaining experiments. Oral endotracheal intubation was performed routinely and anesthesia was then deepened so that either apnea occurred, necessitating artificial respiration, or controlled respiration could be secured easily and the dog would offer no resistance to the functioning of the apparatus.

In preliminary experiments the periods of artificial respiration ranged from one to six hours. After it was found that gross pulmonary damage was evident within two hours and was as great as that following a six-hour test period, a two-hour period was generally used in the remaining tests. To correlate the changes of pressure produced by the various methods with morphologic changes which might occur in the lungs, recordings were made of the "oral," bronchiolar (pulmonary), and intrapleural pressures by connections to three separate mercury manometers. The "oral" pressure was obtained by attaching rubber pressure tubing from a manometer to a side arm adapter at the proximal end of the endotracheal tube, that is, it was the pressure existing in the endotracheal tube at the level of the buccal cavity. The pulmonary pressure was obtained by inserting a No. 10 French ureteral catheter through the endotracheal tube into the respiratory tree until resistance was encountered and then withdrawing the catheter slightly to permit freedom of the distal end in a bronchiole. Then each catheter was connected to its manometer. Intrapleural pressure was obtained by inserting into the pleural cavity a trocar of arrowhead shape which had been previously connected to the third recording manometer. The time was recorded on all graphs at six second intervals. Continuous records were made during many of the experiments.

Some of the methods investigated involved the use of positive pressure only, others a combination of alternating positive and negative pressure. These methods* were:

1. Manual pressure on a five-liter rubber bag
2. Manual pressure on the thoracic wall
3. A two-phase (positive-negative pressure) type of resuscitator
4. The Kreiselman bellows
5. The Neff-Lind apparatus
6. A Drinker type of respirator
7. A windshield wiper type of respirator
8. The Eve rocker method

A closed absorption system was used in the first method in which the lungs were inflated by means of intermittent manual pressure on a 5 L. bag, a canister containing soda lime for the absorption of carbon dioxide being interposed between the bag and the endotracheal tube. In the second method the

*After completing this paper an important article has appeared.[12] It deals with still different devices for applying artificial respiration and with other phases of the general problem of their effects on respiratory exchange. The findings are entirely in harmony with this report.

operator's thumbs extended just beneath the level of the diaphragm and the palms of the hands applied intermittent pressure on the lateral chest wall. The two-phase (positive-negative pressure) apparatus[8] has valve controls adjusted at the factory so that the machine is said to operate at a positive pressure of 17.6 cm. of water (+13 mm. Hg) and at a negative pressure of 12.18 cm. of water (−9 mm. Hg). The Kreiselman bellows[9] has an exhalation valve so that only positive pressure may be exerted. In addition, a safety valve functions in connection with a pressure gauge which is adjustable to permit regulation of the maximal positive pressure which may be exerted. The apparatus recently devised by Neff and Lind[10] consists of a rubber bag connected with a metal cylinder which contains a lever so balanced that alternately either end of the lever covers outlets approximately 1 cm. in diameter. When gases pass from the bag to the subject, the exhalation aperture is closed and inflation of the lungs is accomplished. With release of pressure on the bag, the exhalation valve is opened by a tipping of the lever in the opposite direction. A pressure gauge and safety valve to limit maximal possible pressure also are present in this apparatus. The form of respirator described by Drinker and McKhann[11] permits the production of pressure on the external surface of the animal (with the exception of the head) and can be adjusted to operate with intermittent positive pressure, intermittent negative pressure, or alternately with each phase. The windshield wiper device supplies intermittent positive pressures within the air passages and can be adjusted to permit pressures as high as +50 mm. of mercury. In the Eve method a support serves as a fulcrum beneath the board on which the animal is fastened, thus permitting alternate elevation of the cephalic or caudal end at 45 to 50 degrees from the resting horizontal position.

Each of the eight methods was used separately on at least six different animals and several of the methods were tested on ten or twelve dogs. The pressures at which the various devices were used were determined by the amount deemed necessary for adequate ventilation of each animal as determined by thoracic expansion and oxygenation of the blood. No flexibility in operation of the two-phase type of respirator (No. 3) was possible.

To be certain that adequate oxygenation of the blood was being accomplished by each method of artificial respiration, in representative cases analyses of the oxygen and carbon dioxide in the blood were made by means of the Van Slyke technique. The color of the margin of the tongue in individual animals closely corresponds to the degree of oxygenation of the blood and therefore this area of vascularity was continuously observed in all experiments. Oxygen was used as the respiratory atmosphere in certain of the tests, and air in the remainder. Direct blood pressure recordings were made in some of the experiments. No premedicating drugs were ever used. Animals were tested in the following ways:

A. A group of animals not subjected to experiment was sacrificed by the intravenous injection of 2 Gm. of nembutal at such a rapid rate that death occurred between one inspiration and the time when the next should have appeared. As was evident from electrocardiograms, not more than six cardiac cycles occurred before there was cardiac arrest.

B. Animals in one group were anesthetized, their tracheas intubated, and they were allowed to breathe spontaneously for two hours before being sacrificed.

C. Animals were tested by one of the methods of artificial respiration for two hours and then permitted to recover.

D. Animals were sacrificed directly at the close of the period of artificial respiration.

E. A group of animals was subjected to a period of artificial respiration and then allowed to recover for periods of two to twenty-four hours before being sacrificed. Most of the recovery periods were for less than four hours.

Groups A and B served as controls for the other groups, in each of which animals were subjected to the various methods of artificial respiration. Gross examinations of the lungs of all animals except those of Group C were made immediately following their sacrifice. The majority was killed as described. In a few instances citrate solution was administered intravenously or the animals were exsanguinated. From any area of the lung which appeared abnormal, blocks of tissue were obtained and fixed in 10 per cent formalin. When no gross damage was evident, tissue was taken from each lower lobe, the hilum of each lung, and from one apex. Microscopic study was made of all such tissue. The gross and microscopic studies were done in consultation with, and under the direction of, a member of the department of pathology.

In some cases, just prior to the opening of the thorax, the lungs were inflated moderately and the trachea clamped. Occasionally the lungs were removed in toto and were submerged in water to determine if there had been any peripheral rupture or if there was atelectasis. The location of the distal end of the bronchiolar catheter was checked routinely in animals sacrificed immediately and was always found to be within 1 cm. of the periphery of a lower lobe. Inspection also was made to determine if any damage had been caused by the intrapleural trocar.

RESULTS

Blood Pressure and Blood Gases.—No significant alterations occurred in the direct blood pressure recordings during routine use of any method. Usually adequate oxygenation of the blood was produced in each experiment. In a few instances, and only with the Drinker type of respirator, adequate oxygenation could be accomplished only when the atmosphere was enriched with oxygen. In the experiments with animals more lightly anesthetized, in which hyperventilation was used intentionally to gain *control* of the respiration, the reduction of carbon dioxide in the blood was not found below 40 volumes per cent. Since analyses showed that both the oxygen and carbon dioxide content of the blood were within normal limits, it is not believed that there was any significant alteration of acid-base balance.

Sacrificing of Animals.—The method of sacrificing animals used in studies of pulmonary damage is very important. The quickest possible respiratory and cardiac arrest is necessary to avoid excessive pulmonary congestion. In a few instances when the animal's heart was found to be active after the thoracic cage was opened, or when it took some "dying gasps," marked changes were observed in the lungs. Under these circumstances if the lungs were pink, crepitant, and normal at the moment of exposure they almost immediately underwent a spectacular change, became markedly congested, and appeared almost like liver. Microscopically, it was found in such cases that the chief abnormality was an intense congestion. There was never any noticeable secretion or presence of mucus in the respiratory tree in any of the experiments. The pulmonary damage occurring in animals whose lungs had been inflated with air or oxygen was much the same.

Changes of Pressure.—During spontaneous respiration the positive "oral" and bronchiolar pressures changed by approximately 1 to 5 mm. Hg. The

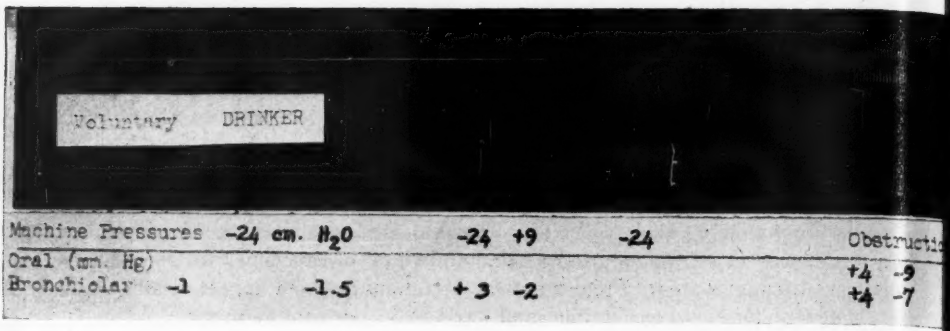

Fig. 1.—In all records the upper line represents "oral" pressure, the second line pulmonary (bronchiolar) pressure. The very first portion of this tracing records a depressed animal's spontaneous respiration, the "oral" pressure not being great enough to appear on the graph. The Drinker type of respirator was set to perform in one instance at a negative pressure (−24 cm. H_2O) and at another time at negative-positive pressures (−24 to +9), as shown on the line of machine pressures. The changes in bronchiolar pressure are readily seen, but still the "oral" pressure is barely visible on the tracing. Mechanical obstruction by clamping the endotracheal tube produced an abrupt rise in both the "oral" and the bronchiolar pressures.

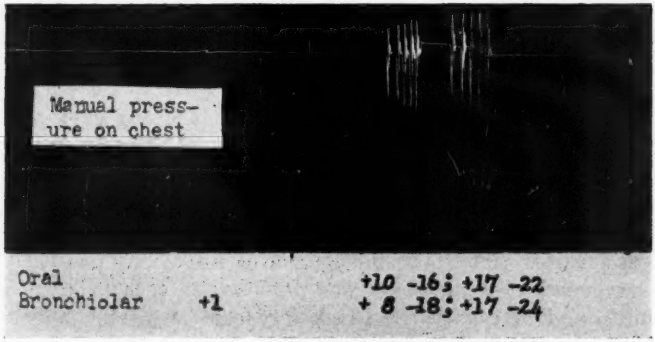

Fig. 2.—Records from manual pressure on the chest. "Oral" and bronchiolar tracings are as in Fig. 1. The low pressures obtained by this method are comparable with those of spontaneous respiration in Fig. 1. Again it can be seen how mechanical obstruction markedly increased the pressures.

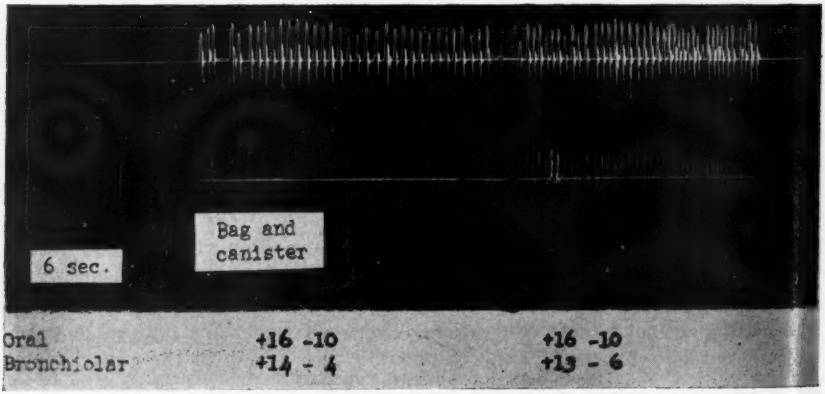

Fig. 3.—This graph shows pressure effects with "controlled respiration" by intermittent pressure on a bag (absorption technique). The pressures could easily be varied to suit the demands of the animal by changing the amount of manual pressure exerted on the bag, and by varying the degree of distention of the bag with gas. Relatively higher pressures were exerted here than in the methods in Figs. 1 and 2.

same magnitude of change occurred in the application of manual pressure on the chest, by use of the Drinker type of respirator, and by the Eve method. The greatest change in positive pressure which occurred with the operation of any machine was +34 mm. Hg in the "oral" and +28 mm. Hg in the bronchiolar system. When mechanical obstruction was produced by blocking the outlet of the endotracheal tube for several respiratory cycles, the positive "oral" and bronchiolar pressures became as high as +76 mm. Hg. Thus, spontaneous efforts of the animal during intentional obstruction created much greater

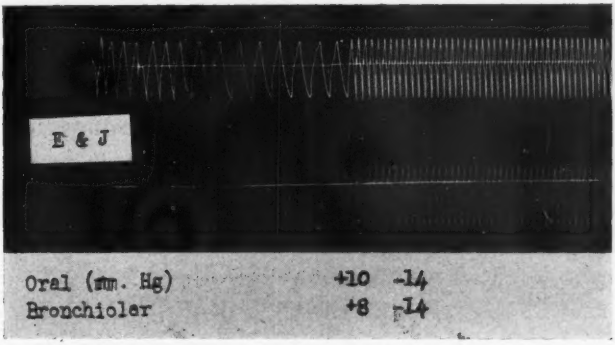

Fig. 4.—The uniformity of pressures produced by the two-phase type of respirator is well represented in this graph. This machine exerts both positive and negative pressures in the alveoli. The negative pressure (suction) produced by this method is comparatively greater than that found with any other method. The change in rate of respiration was managed by the operator of the machine.

Fig. 5.—On this recording it can be noted that with the "windshield wiper" apparatus there is a constant positive pressure being exerted, upon which respiratory pressure fluctuations are superimposed. Despite the relatively high positive pressure, no exceptional pulmonary damage was produced.

changes of pressure than any of the mechanical devices. The greatest negative pressure also was obtained by obstruction of the endotracheal tube during spontaneous exchange and again greatly exceeded that produced by any machine. It amounted to −35 mm. Hg in both the "oral" and bronchiolar manometers.

Figs. 1 to 9, as presented with their legends, give graphically the relative changes of pressure recorded. Exact values are not considered as significant, but the relative differences in the pressures which are created in using the various methods are, we believe, significant. "Oral," bronchiolar (pulmonary), and intrapleural pressures are designated in millimeters of mercury

from the direct manometric readings. As indicated in the legends of some of the figures there was frequently a definite negative phase created in the proximal end of the endotracheal tube ("oral" pressure) by sudden release of pressure on the rubber bag. At other times, inertia of the mercury column of the manometer created an artefact simulating such a condition. Inspection of the graphs during their recording and before photographic reduction permitted determination of the true state at this site. All recordings of intra-

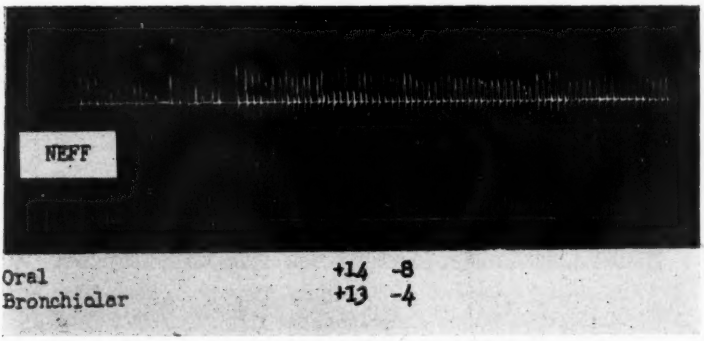

Fig. 6.—With the Neff-Lind apparatus (intermittent positive pressure is produced in the alveoli by moderate manual pressure on a rubber bag), pressures most similar to those found in Fig. 3 were obtained. This is a positive pressure open method. A portion of the apparent negative "oral" pressure was an artefact due to bounce of the Hg column when the bag was suddenly released by the hand of the operator.

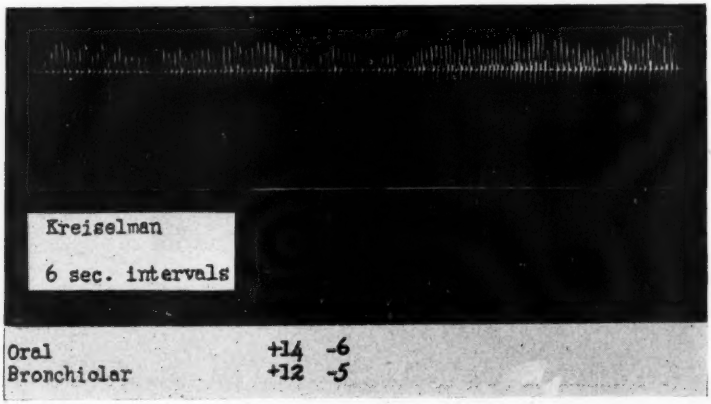

Fig. 7.—The pressures recorded here with the Kreiselman bellows correspond to those in Figs. 3 and 6. Again, a portion of the negative "oral" pressure is due to inertia of the Hg in the manometer. The time recording is shown here as was the case in Fig. 3.

pleural pressure showed it to be negative. These readings were checked by graphic recording during the insertion and removal of the trocar. Since no base line was used for this manometer, no pressure sign is indicated for the intrapleural values in Figs. 8 and 9.

Histologic Changes.—The lungs from a few of the control animals, on gross inspection, appeared more nearly normal than those from the animals of the experimental groups. Microscopically, no differentiation was possible. *No one method was superior* to another in so far as failure to cause pulmonary changes

was concerned. There was not a single section which did not show some evidence of abnormality. The sections of lung from the control animals, either those killed immediately or after a period of anesthesia equivalent to that in which methods of artificial respiration were applied, contained the same types of damaged tissue as those taken from animals in which the manipulations of

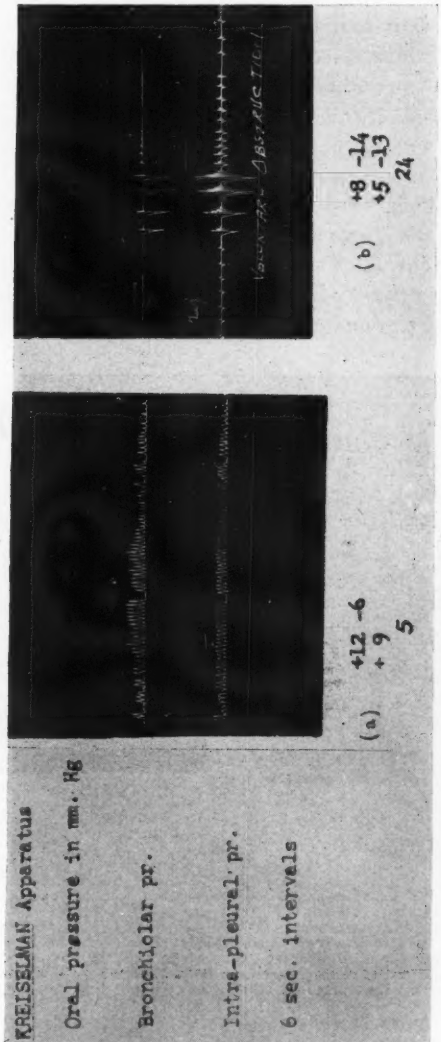

Fig. 8.—These tracings have been selected to show the additional recording of intrapleural pressure, which is the third line of the graph and also was directly recorded from a mercury manometer. All the readings of intrapleural pressure are negative but no base line was added, hence they are not so designated. (*a*) This is a record when the Kreiselman apparatus was in use. Here a definite negative "oral" pressure occurred. (*b*) This record was made during spontaneous respiration and it shows how pressures are progressively increased when free exchange of gases is prevented by obstructing the endotracheal tube.

artificial respiration were employed. Thus, such minimal changes can be assumed practically always to exist in the normal (pre-experimental) state even when animals are sacrificed by the speediest method possible and with no period of anesthesia or artificial respiration.

The histologic findings included partial to marked atelectasis, congestion, bronchial and alveolar hemorrhage, bronchiolar spasm, edema, emphysema, and occasionally pneumonic patches. The most common findings were partial

atelectasis and congestion. More congestion was found in the lungs of the animals which were not rapidly sacrificed, but which made a few "dying gasps," or in which the heart continued to beat after exposure. The emphysema occurred in those lungs in which higher pressures were exerted for most of the test period, and not in those in which a high pressure was produced temporarily by obstruction. No rupture of the visceral pleura nor any internal pulmonary rupture was ever found. The pneumonic patches are considered to have been due to previous infection in the dogs rather than to have developed during a two-hour period of artificial respiration.

Since there were essentially the same types of morphologic changes found in the lungs of the two control groups of animals (A and B) as in those in which artificial respiration was continued for two to six hours, the animals of Group C were given artificial respiration for two hours and then replaced in their kennels. Not only did they respond very quickly but the post-treatment period was entirely uneventful. The animals of Group E were sacrificed after recovery periods of two to twenty-four hours and their lungs appeared grossly normal. Microscopically, minimal changes were found which were practically

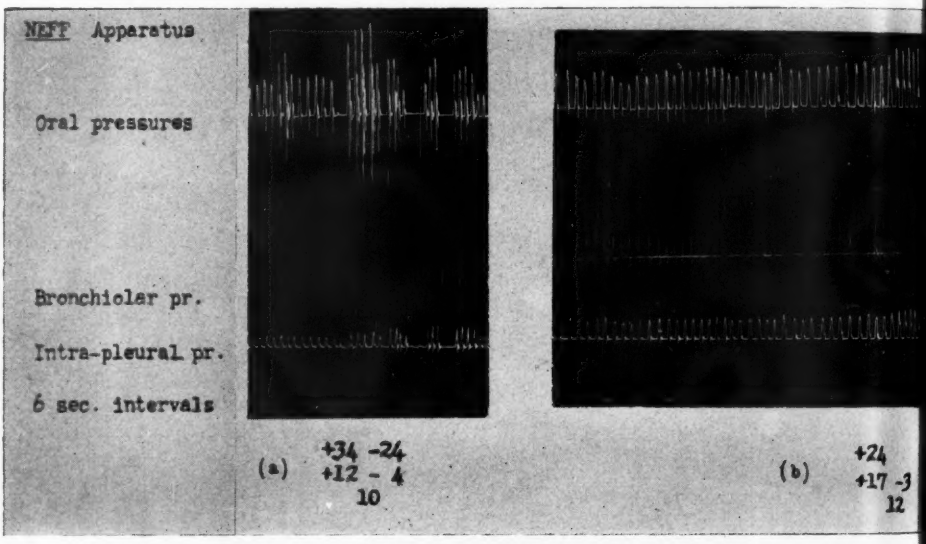

Fig. 9.—Using the Neff-Lind apparatus, it was possible (*a*) to increase pressures to levels corresponding to those which occurred during obstruction. The only safeguard against such high pressures is the control the anesthetist exercises in the amount of pressure which he exerts on the bag. In (*b*) the negative pressure has been reduced or eliminated by a slower release of pressure on the bag by the operator. This effect should be compared with that seen in Fig. 6.

identical with those of the control groups. Moreover, since no significant increase in damage occurred by a lengthening of the period of artificial respiration, such manipulation could not be judged to be a highly significant factor in the production of morphologic changes. The changes which did occur in the lungs were definitely reversible and recovery could be expected in all cases after a few hours.

For the last thirty-eight experiments an arbitrary gradation scale was set up to correlate the pathologic findings, as noted in Table I. Arabic numbers 0 through 6 refer to increasing degrees of gross damage; Roman numbers I

through V refer to the degree of damage of tissue seen microscopically. No significant correlation of degree of damage with respect to the method used is at all evident in either the gross or microscopic tabulation. The earlier tests had results similar to those found in the last thirty-eight experiments.

TABLE I. RESULTS OF EXPERIMENTS ON THIRTY-EIGHT ANIMALS

METHODS OF ARTIFICIAL RESPIRATION	NO. OF ANIMALS	DEGREE OF DAMAGE											
		GROSS LESIONS*							MICROSCOPIC LESIONS†				
		0	1	2	3	4	5	6	I	II	III	IV	V
Total, 7	38												
Drinker	6		1‡		4	1				1‡	3	1	1
E. & J.	7	1‡§	3		1‡		2			2	2	1	1
Neff-Lind	7		2§	4§			1			2	1	1	1
Manual on chest	3				1		1	1			1	2	
Manual with bag and canister	2		1	1							2		
Windshield	3	1	2							2	1		
Kreiselman bellows	2			2							2		
Sacrificed (no artificial respiration)	6		3	1	1			1‖		3	3		
Not sacrificed	2	Uneventful recovery											

*Degrees of damage, *gross lesions:* 0, No damage; 1, no hemorrhagic patches over 2 cm. and total area involved not over ½ of one lower lobe; 2, hemorrhagic areas over 2 cm. but total <1 lobe; 3, total involved area <25 per cent of total lung parenchyma; 4, total involved area <50 per cent of total lung parenchyma; 5, total involved area >50 per cent but less than 75 per cent; 6, total involved area >75 per cent of total lung parenchyma.

†Degrees of damage, *microscopic lesions:* I, No damage; II, minimal involvement; III, moderate involvement; IV, severe involvement; V, extreme involvement.

‡After recovery period.

§No microscopic examination, one animal in each group.

‖100 per cent congestion.

Experiments by the Eve method were done before this classification was employed but would have compared closely with the results of the windshield method.

DISCUSSION

Probably the most outstanding feature of this study was the fact that there was evidence of abnormality in every section of lung examined. Tissue from both control groups (A and B) had similar morphologic changes to those found in the experimental groups (D and E), although not to as great an extent. The fact that a six-hour period of artificial respiration caused no more significant change than did a two-hour period offered proof that time was not an important factor. If, however, a recovery period was allowed, the pathologic findings were diminished over a period of a few hours.

Undoubtedly the question of the use of air versus oxygen needs further investigation. Although we are unable to make a positive statement favorable to either one, morphologic changes due to the gaseous content of the atmosphere have not been ruled out. No evidence was found that the anesthetic agent, per se, affected our findings.

The variability of the recordings of pressure compared with the pathologic findings was somewhat surprising. The same pathologic changes were observed whether minimal or maximal pressures had been applied. Actually, if any correlation is possible from Table I, the least evidence of abnormality was obtained with the windshield wiper apparatus, with which positive pressure was maintained throughout the respiratory cycle. However, with this particular piece of apparatus, one may doubt the physiologic completeness of expiration and it leaves open the possibility of the effect of constant positive pressure on the circulation. Undoubtedly there is an impediment to venous return in the greater circulation and an increased demand on the right ventricle to maintain pulmonary circulation. The entire condition might be quite different in a person near death, for example from drowning, where the circulation as well as the respiration had been impaired before artificial respira-

tion was instituted, and where muscle tonus was greatly decreased or absent.[7] No difference was evident when the Eve method was applied under conditions comparable to those used for the other methods.

Each of the methods of artificial respiration had peculiarities and difficulties to which the operator had to become accustomed. Resuscitators with valves adjusted to release at set pressures did not always do so. Hurtle manometers were used to check the mercury manometers. Occasionally valves would become stuck at their maximum or minimum position. Had an operator not been present to correct the error the animal would have been lost from cessation of respiratory exchange. With one piece of apparatus the metal valve parts became completely disassembled during an experiment. Levers in some machines were not balanced delicately enough to tip from the inspiratory to the expiratory position. Again, during the course of experiments, some machines entirely ceased to function and a new method had to be employed. Occasionally motors became overheated and there was forced discontinuance of use of the machine. In fact, there was not a single mechanical device which did not offer difficulties at times. The more elaborate mechanical machines are naturally quite costly. Some of the methods are much more fatiguing than others when artificial respiration is administered for several hours. These factors all have some importance, but the paramount thought in all cases must be the production of safe and adequate ventilation for the suffocated person or for one whose respiration is depressed. This should be done by whatever method is *immediately* available and most successful in the hands of a particular operator, and that which does the least amount of damage to the patient's lungs and circulation. Clinical confirmation of this study is now in progress.

SUMMARY

1. Pulmonary abnormalities were present in control groups of animals either sacrificed and examined without any period of anesthesia or respiratory manipulations, or subjected only to anesthesia, during which respiration occurred spontaneously. Similar morphologic changes were evident in groups of animals subjected to various methods of artificial respiration.

2. In all groups, regardless of method, duration of artificial respiration, or anesthetic drug used, histologic examination showed areas of atelectasis, congestion, hemorrhagic infiltration, and bronchial spasm.

3. Animals sacrificed after a two- to three-hour recovery period following the period of artificial respiration had no gross pulmonary changes and had minimal microscopic pulmonary abnormality which was equivalent to that present in the control groups.

4. Any damage which did occur in the lungs was reversible since all dogs that were permitted to recover did so without sequelae.

5. In studies of pulmonary damage, animals should be sacrificed by a method which causes almost instantaneous cardiac and respiratory arrest.

6. This study does not permit any final statement as to the degree of damage produced by inflation of the lungs with air as compared with oxygen.

7. No significance is claimed for the exact values for changes of pressure produced in the various methods, but relative differences were quite definite.

8. The maximal changes of pressure in the lungs recorded in this study were produced during spontaneous respiration when the endotracheal tube was obstructed. The maximum positive pressure so recorded was +76 mm. Hg and

the negative −35 mm. Hg. The greatest changes of pressure by any of the methods of artificial respiration were not more than one-half of those which the animals produced spontaneously during brief periods of obstruction.

We are grateful to Dr. J. C. McCarter and Dr. Gorton Ritchie, associate professors of pathology, for advice and confirmation throughout this study. Dr. W. Vernon Lee aided in the early phases of the investigation.

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LUNG ABSCESS CAUSED BY BACTEROIDES NECROPHORUS

Report of a Case With Autopsy

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SPONTANEOUS infections with *Bacteroides necrophorus*, occurring in domestic animals and birds and producing an acute type of necrotizing inflammation of the mucous membranes, skin, lungs, and liver are well known to veterinarians.[1-3] Human infections with this organism, although rare, have been reported. The disease in man has manifested itself by a primary lesion on the skin following trauma, or on the mucous membranes, usually the posterior nasopharynx or larynx. Dissemination by way of the blood stream may occur from an original focus of infection causing abscesses in the liver, lungs, joints, and subcutaneous tissues. The pathologic changes produced by this organism in the tissues are characterized by foci of acute inflammation which undergo liquefaction necrosis. Large clusters of pleomorphic forms of the bacteria are seen near the margin of the necrotic foci. In the tissues the organism may appear as a small coccobacillus or as a filamentous form with occasional branch-

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ing.[4] *Bacteroides necrophorus* belongs to the group of nonsporulating anaerobic bacteria described in the literature under *Bacterium necrophorum, Bacillus funduliformis,* and *Actinomyces necrophorus.*[4] Careful comparative studies of various strains of these organisms have shown no significant differences in their properties. Moreover, the pathologic changes produced in man are essentially the same for all the strains studied.[5] Our reasons for the selection of the name *Bacteroides necrophorus* will be discussed in the section on bacteriologic studies.

Because of the frequency of infections with *Bacteroides necrophorus* in cattle, swine, and sheep the importance of the disease in man as an occupational hazard cannot be overlooked. Instances of infections in veterinarians and meat inspectors have been reported, but in all the disease has remained localized in the skin.[6, 7] Although the usual primary focus is in the skin, lesions in the nasopharynx and larynx lend support to the assumption that air-borne or droplet infections may occur. In the case to be reported the patient's occupation as a wool and fur buyer brought him into contact with the green hides of cattle and sheep, which we feel was the source of infection. The history of a sore throat, which subsequently disappeared, followed by signs of pulmonary disease and the subsequent development of a lung abscess lends strength to the idea that the infection was air-borne. This case is considered significant not only because it is the first reported instance of primary lung abscess caused by *Bacteroides necrophorus,* but also it is unusual in that the infection remained localized to the lungs.

REPORT OF CASE

A 41-year-old married white man (Barnes Hospital No. 105687) entered the hospital May 28, 1943, and died July 8, 1943.

Chief Complaints.—The patient complained of a productive cough and fever of three months' duration and loss of thirty-five pounds over the same period of time.

Social History.—The patient was born in Texas and had lived in that state all his life. For many years he had been in the wool and fur business and at the time of his illness was a buyer, which occupation required him to handle the hides and inspect them closely. Consequently, he was in close contact with wool and mohair, as well as green cowhides and the rawhides of all fur-bearing animals in Texas. He smoked one to two packages of cigarettes daily and stated that he occasionally drank whiskey to extremes before his illness.

Past History.—His past health had always been good. When a child he had measles, mumps, and whooping cough without any known complications. In 1935 he had gonorrhea but it cleared up with treatment by a physician. He received a total of thirty-four hip injections over a two-year period although there was no history of a primary lesion or a positive serologic test for syphilis. He also stated that his tonsils had always been bad and that he had an attack of tonsillitis and sore throat every three to six months.

Illness on Admission.—In February, 1943, the patient stated that he developed a severe "sore throat" and a "cold" in his chest. He did not consult a physician at this time but remained in bed and took one of the sulfonamide drugs. After four days the fever subsided and he resumed his work, although a dry cough persisted. A few days later he again developed fever, so returned to bed and took one of the sulfonamide drugs. He remained in bed for two weeks and then resumed his regular work. He was forced to bed a third time because of weakness, fever, and a persistent cough. On March 21, the cough became much worse, being productive of one-half cup of purulent material a day, occasionally flecked with blood. He also noticed some deep pain in the right side of the chest and consulted a physician who took a roentgenogram, which was reported as showing "clouding" in the right side of the chest. The cough, which had been present since the onset of his illness, was worse at night. The fever was low grade in the beginning and usually occurred in the afternoons. On March 28, the patient entered the Scott and White Clinic at Temple, Texas. On admission it was noted that his finger and toenails were markedly curved in both diameters. Physical examination of the chest revealed dimunition in tactile fremitus posteriorly over

the right chest, especially in the subscapular region. The breath sounds were also diminished in this area. Examination of the urine on admission was negative. The white blood cells ranged between normal and 17,000 per. c.mm. The sedimentation rate was 83 mm. per hour. The Wassermann reaction of the blood was negative. Agglutination tests for typhus fever, undulant fever, typhoid, and tularemia were negative. Examination of the sputum was negative for acid-fast organisms. A roentgenogram of the chest revealed a shadow in the right chest and bronchograms showed occlusion of the "right dorsal root bronchus." Several bronchoscopic examinations were performed and revealed large amounts of purulent material in the bronchial tree and occlusion of the "right dorsal root bronchus." The patient's fever did not respond to chemotherapy. He continued to cough up large amounts of purulent sputum. A mild secondary anemia developed and a blood transfusion was given, May 24. Because of the occlusion of the "right dorsal root bronchus" and the shadow demonstrated by roentgenograms in the right lung it was felt that bronchogenic carcinoma should be considered, therefore the patient was referred to the chest service at Barnes Hospital for diagnosis and treatment.

Physical Examination.—On admission the patient was a well-developed and fairly well-nourished man, who coughed almost continually. His temperature was 39.3° C. There was no generalized enlargement of the lymph nodes. His breath had a foul odor and the teeth were dirty and carious. The pharyngeal tonsils were enlarged and cryptic and a yellowish exudate was present on the left tonsil. Examination of the chest revealed a respiratory lag on the right side. On percussion there was dullness to flatness over the entire lower three-fourths of the right chest with slight hyper-resonance on the left. Breath sounds were absent over the area of dullness and tactile fremitus was diminished over the same region. Above the area of dullness, the breath sounds were bronchial in character. The left side of the chest was clear to percussion and auscultation. The heart was not enlarged and the rhythm was regular. The pulse was 88. The rest of the physical examination was essentially negative.

Laboratory Data.—On admission the urine showed a specific gravity of 1.004 and a slight trace of albumin. The red blood cell count was 3.76 million per cubic millimeter and the hemoglobin 10 Gm. The white blood cell count was 11,300 and the differential count showed 22 stabs, 64 segmented forms, 10 lymphocytes, and 4 monocytes. The red blood cells were reported as being slightly hypochromic and the platelets were considered adequate. The nonprotein nitrogen was 15 mg. per cent and the fasting blood sugar 93 mg. per cent. The Kahn reaction of the blood was negative. The total serum protein was 5.3 Gm. with 3.2 Gm. of albumin and 2.1 Gm. of globulin. Repeated examinations of the sputum were negative for acid-fast organisms and for fungi. The vital capacity was 1,800 c.c. An electrocardiogram was reported as indeterminate. Roentgenograms of the chest showed an opacity on the right side which obscured the lung markings between the anterior ends of the third to the sixth ribs. Lines were seen, which were considered suggestive of a fluid level. The interpretation was infiltration in the lower lobe of the right lung with abscess formation.

Course in the Hospital.—A diagnostic bronchoscopy was performed three days after admission and much thick, greenish-yellow pus, with a foul odor, was seen in the trachea. The wall of the right lower lobe bronchus was thickened and a biopsy was taken. Samples of the purulent exudate in the trachea were inoculated into guinea pigs and sent to the laboratory for culture. Because of the large amounts of purulent material in the bronchial tree, the first bronchoscopic examination was considered unsatisfactory and a second was performed, June 7, on the ninth hospital day. No tumor was seen but several small bits of tissue were removed for microscopic study. The pathologic reports on the biopsies were chronic inflammation. Because of the nature of the lesion it was deemed advisable to give the patient a course of x-ray therapy over the right lung before an attempt at drainage was undertaken. Five hundred roentgen units were given to the anterior and to the posterior aspects of the right chest. The patient received three transfusions, each with 500 c.c. of whole blood. June 24, on the twenty-seventh hospital day, a right cautery pneumonotomy was performed by Dr. Evarts A. Graham. A posterolateral incision was made over the eighth interspace and the posterior one-half of the eighth and ninth ribs was resected. The parietal pleura was found to be very thick and indurated. Aspiration revealed an abscess cavity in the posterior part of the lower lobe of the right lung. The cavity was opened with a small cautery and a large amount of foul-smelling, purulent material escaped. The incision was then carried anteriorly and a larger cavity opened into. It was felt that this was an empyema cavity having a direct communication with the lung abscess. Cultures taken from the pus grew fusiform bacilli, pneumococci, and anaerobic streptococci. No

fungi were recovered. The patient's postoperative course was progressively worse. For the first three days he bled rather profusely from the operative wound and from the bronchial tree, coughing up large quantities of blood. Fluids and repeated blood transfusions were administered but little improvement was observed. Intravenous sulfadiazine had no effect on the fever. July 6, he became comatose and a lumbar puncture was performed. The fluid was clear and no cells were present. The Pandy was negative and determinations for sugar and chloride were within normal limits. He was placed in an oxygen tent, but despite blood transfusions, intravenous sulfadiazine, and fluids he expired quietly, July 8, 194-, on the forty-first hospital day.

Autopsy (Washington University Department of Pathology, No. 10628).—Post-mortem examination was performed one hour after death. Permission was limited to the examination of the thorax and abdomen. There was an open wound of the right chest at the level of the eighth rib which was packed with iodoform gauze. This operative wound was in direct communication with a large abscess cavity in the lower lobe of the right lung. No free fluid was encountered in the pleural cavities. The visceral and parietal pleura was densely adherent around the margin of the operative wound and there were numerous fibrous pleural adhesions over the entire right lung and at the apex of the left lung. The large abscess cavity measured 6 by 7 by 4 cm. and contained a thick, tenacious, greenish-yellow, foul-smelling purulent material. The wall was composed of dense fibrous connective tissue which on cut section measured 6 mm. The weight of the lungs was increased, being 1,620 Gm. The right lung was much heavier than the left, being firm and noncrepitant throughout. In the left lung numerous, irregularly outlined foci of consolidation could be felt. The trachea and bronchi contained a large amount of thick purulent material, similar to that present in the large abscess in the right lower lobe. On cut section through the lungs, abscesses were present in all lobes but were less numerous in the lower lobe of the left lung. They varied from 2 to 12 mm. in diameter and contained a thick, tenacious, yellow purulent material. The abscesses in the right lung were considerably larger than those in the left lung. In the middle lobe of the right lung, near the hilum, there were numerous areas of cavitation which contained a yellow, caseous material. There were numerous grayish-yellow, irregularly defined foci which were firm and slightly elevated above the surrounding lung tissue. These were interpreted as regions of organizing bronchopneumonia. The bronchopulmonary and tracheobronchial lymph nodes were enlarged, some measuring 4 cm. in diameter, and on cut section were grayish-pink, bulging from the surface.

The spleen was enlarged, weighing 487 Gm. The organ was soft and flabby. On cut section the splenic pulp could easily be scraped from the surface with the knife. The trabeculations were prominent and appeared as small grayish-white strands.

The liver was also enlarged, weighing 2,320 Gm. The surface was smooth but the entire organ was discolored a light yellow, which on cut section was evenly distributed throughout the parenchyma. The central regions were prominent and dark reddish brown, giving the substance of the liver a mottled appearance.

Gross examination of the other viscera revealed no abscesses or pathologic changes related to the disease in the lungs.

Microscopic Examination.—A section of the large abscess in the lower lobe of the right lung showed the abscess wall composed of dense fibrous connective tissue. Adjacent to this was a layer of fibrin which contained large clusters of gram-negative pleomorphic bacteria. Near the center of the clusters they appeared as small coccobacilli, while at the periphery and in the surrounding tissue there were filamentous forms which contained small, densely staining granules. In the lung tissue surrounding the abscess the alveoli were filled with a fibrinous exudate which contained a few polymorphonuclear leucocytes. In many of the alveoli the exudate was beginning to undergo organization. The alveolar septa were greatly thickened and the lining epithelium was composed of tall columnar cells, which in many places had become pseudostratified. In some parts of the section the alveolar walls had undergone necrosis. At the margin of the necrotic foci large clusters of bacteria surrounded by polymorphonuclear leucocytes, plasma cells, and lymphocytes were seen. The bronchioles were filled with many polymorphonuclear leucocytes and scattered lymphocytes. This bronchial exudate also contained many clusters of blue-staining bacteria. The bronchial mucosa was for the large part disintegrated, but in certain areas there was metaplasia with transformation to stratified squamous epithelium. Scattered diffusely throughout the lung tissue were many large macrophages filled with a light brown pigment.

A section from the middle lobe of the right lung showed lesions which appeared somewhat older than those in the remaining lobes of the lungs. There were numerous small cavities which were surrounded by fibrous connective tissue and contained a necrotic material within which numerous bacteria could be seen. There was thickening of the alveolar septa and metaplasia of the lining epithelium. The alveoli were filled with an organizing exudate and only an occasional polymorphonuclear leucocyte was seen. The blood vessels were dilated and engorged with red blood cells. The walls of the arterioles were thickened and there was proliferation of the endothelium but to a much less degree than that seen in other parts of the lungs.

Sections from the other lobes of the lungs showed similar pathologic changes consisting of thickening of the alveolar walls, a fibrinous exudate within the alveoli containing a few polymorphonuclear leucocytes, and a moderate amount of edema fluid. In the abscessed areas there was necrosis of the alveolar septa and infiltration with numerous polymorphonuclear leucocytes, lymphocytes, and plasma cells. Usually in the center of the small abscesses large clusters of bacteria were present, but in the larger areas of abscess formation

Fig. 1.—Large abscess in the lower lobe of the right lung; small abscesses in the other lobes of the lungs with the distribution suggesting a bronchogenic spread.

there was liquefaction necrosis. The reaction in the small arterioles was quite impressive, consisting of thickening of the walls and infiltration with polymorphonuclear leucocytes. There was a marked proliferation of the intima, which in some instances almost occluded the lumen. Within some of the medium-sized veins there were partially organized thrombi and the same type of cellular infiltration within the walls as was seen in the arterioles. Throughout all sections of the lungs there were numerous large macrophages filled with a brown-yellow pigment. These macrophages were seen diffusely scattered throughout the substance of the lung but were also present in small focal collections. Zenker-formol-fixed blocks of all lobes of the lungs and of the wall of the large abscess in the lower lobe of the right lung were embedded in paraffin and sections cut at 3 μ were stained by Goodpasture's

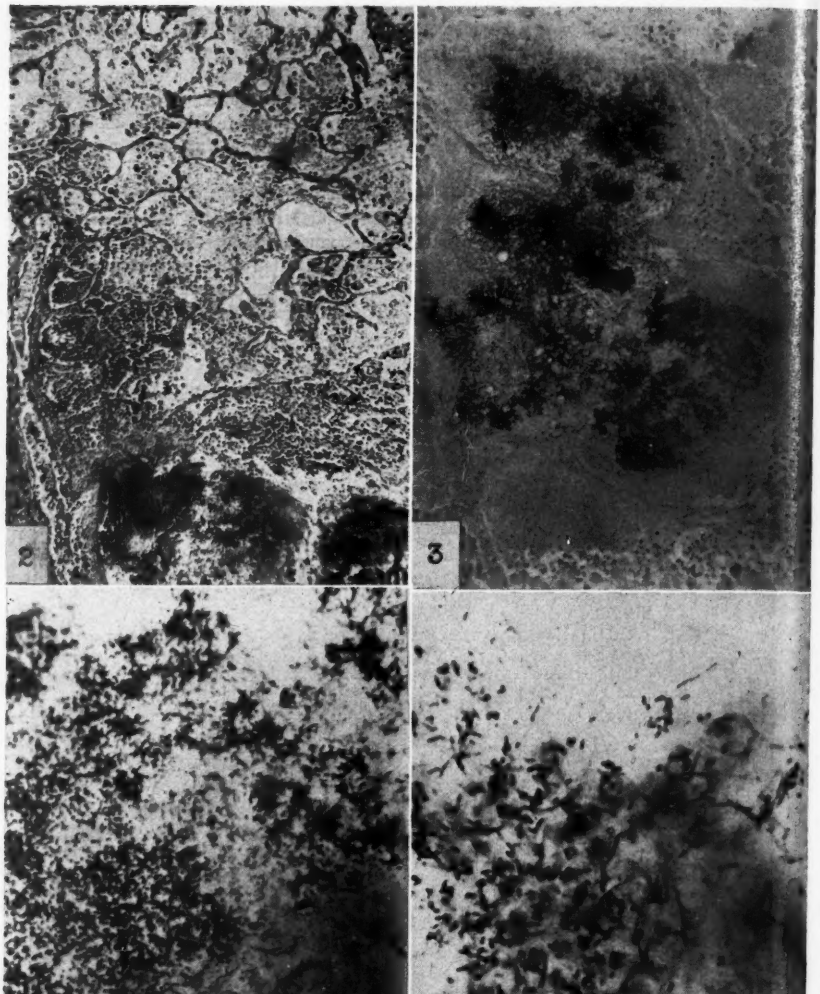

Fig. 2.—Lung parenchyma surrounding necrotic focus, showing cellular infiltration and exudate in the alveoli consisting of fibrin, polymorphonuclear leucocytes with occasional lymphocytes and plasma cells; hematoxylin eosin stain (×135).

Fig. 3.—Large clusters of organisms within a necrotic focus; the pleomorphism is well seen, even at low magnification. Goodpasture's modification of Gram's stain (×135).

Fig. 4.—Bacteria within lung tissue at the edge of a necrotic focus showing the extreme degree of pleomorphism; the organisms in the center of the cluster appear as coccobacilli while near the periphery they tend to assume a filamentous form. Goodpasture's modification of Gram's stain (×570).

Fig. 5.—Higher magnification of the bacteria showing small granulates within the filamentous forms. Goodpasture's modification of Gram's stain (×1100).

modification of the Gram technique. The bacteria were studied most satisfactorily within the small abscesses. With this method of staining, the pleomorphic forms of the organism in tissue were well seen. Where large clusters of bacteria were present they appeared as extremely pleomorphic, gram-negative, thin rods with many filamentous forms. Near the center of the clusters there was a tendency to assume a coccobacillary form, while near the periphery, filamentous forms which contained a regular, deep-staining, coccus-like granulate were the predominating types. Organisms could be found scattered throughout most of the lung substance but were most numerous in the foci of necrosis. Where the bacteria were found singly or in small numbers the filamentous forms predominated. In the foci of necrosis they appeared as small coccobacilli. Zenker-formol-fixed tissue from all lobes of the lungs were embedded in paraffin and the sections were stained by the Ziehl-Neelsen technique. Careful examination revealed no acid-fast organisms.

A section of the spleen showed a dilatation of the sinusoids, which were filled with red blood cells and polymorphonuclear leucocytes. The follicles were large and irregularly outlined. The substance of the spleen contained numerous polymorphonuclear leucocytes and a few scattered eosinophiles. Many large macrophages, containing a light yellow-brown pigment, were also present.

A section of liver showed large vacuoles within the hepatic cells. These vacuoles varied somewhat in size but were most numerous in the central and mid-zonal regions. The sinusoids around the central vein were dilated and contained a moderate number of red blood cells. No necrosis of liver cells was present. The Kupffer cells were enlarged and filled with the same type of brown pigment described in the lungs and spleen.

Sections of the other organs showed no pathologic changes related to the primary disease.

Final anatomic diagnosis: Abscesses of all lobes of the lungs, advanced on the right (*Bacteroides necrophorus* isolated in culture and identified in the tissue); multiple cavitation of the middle lobe of the right lung at the hilum; organizing pneumonia of the right lung; open wound of the right chest with insertion of a drain into an abscess of the lower lobe of the right lung (history of a cautery pneumonotomy, fourteen days); hyperplasia of the tracheobronchial lymph nodes, advanced; fibrous pleural adhesions over the entire right lung and the apex of the left lung; hyperplasia of the spleen; passive congestion of the liver; hemosiderosis of the liver and spleen (history of blood transfusions); fatty metamorphosis of the liver, slight.

BACTERIOLOGIC STUDIES

Sterile cotton swabs were moistened with purulent exudate present in the bronchi. In several areas the pleural surface of the lung was cauterized by a hot spatula and characteristic lesions were exposed by incisions with a sterile knife. Sterile cotton swabs were moistened with purulent material from the lesion, care being taken to swab the peripheral portions of the abscess, and each swab was placed in a separate, sterile tube. In addition, small amounts of the purulent material were collected in sterile Kolmer tubes.

Wet, supravital preparations, faintly stained by Loeffler's methylene blue, diluted 1:100, and fixed smears, stained by modified Gram's method, were examined to determine the types of organisms present. The predominant form in all specimens was a gram-negative, pleomorphic, nonmotile rod; many of the rods were fusiform with blunt ends. Their width averaged 0.5 to 1.5 μ, and the length was subject to considerable variation, some measuring less than 3 μ, others being longer and even filamentous, 10 to 30 μ in length. In some instances the organisms were enlarged at one end, presenting a club-shaped appearance. Generally, the smaller rods were single, but numerous short chains were also present. A few fields contained forms which suggested branching or false branching. In addition to this predominating type there were a few spheroidal bacteria, averaging 1 μ in diameter, and moderately plump, coccobacillary, gram-positive rods, measuring from 1.5 to 2 μ in length.

Portions of purulent material were streaked on two plates of veal infusion agar to which sterile, defibrinated rabbit's blood had been added to a concentration of 5 per cent. Other portions were added to two tubes containing 30 c.c. of tryptose-phosphate broth* with 5 per cent rabbit plasma. One tube and one plate were incubated aerobically at 37° C. and the others were incubated at 37° C. in a phosphorus type, anaerobic jar. The cultures were observed after forty-eight hours and, thereafter, daily for ten days.

Post-mortem blood cultures were made by aseptically removing 10 c.c. of blood from the right atrium and adding 5 c.c. portions to tubes containing plasma-tryptose-phosphate broth described previously. Blood was streaked on two plates of blood agar, containing para-amino benzoic acid, 2 mg. per 100 c.c., and cultures were incubated aerobically and anaerobically. Five cubic centimeters of blood were placed in a sterile Kolmer tube and the separated serum was stored at 5 to 8° C. for future use if indicated. Only a few colonies of *Staphylococcus albus* and *Sarcina lutea* developed on the blood agar plates and no additional organisms were recovered in the blood broth cultures. Because of results obtained in cultures from the pulmonary lesions, the nature of the growth, and subsequent histologic studies, these organisms did not appear to be significant and were regarded as contaminants.

After seventy-two hours, two types of colonies were observed in significant numbers on the anaerobic plates prepared with material from the pulmonary lesions. The one, designated as organism A, occurred in large numbers. The second, less frequently encountered type, designated as organism B, was also found on aerobic plates. In addition to these forms, there were a few colonies on aerobic and anaerobic plates, subsequently identified as *Staphylococcus aureus* and *albus*. Because of the relatively few colonies and the absence or rare occurrence of staphylococci in the histologic sections, they were regarded as secondary invaders or contaminants.

Upon further study of organism A, the characteristics listed here were determined and the organism was identified as *Bacteriodes necrophorus*.

1. *Surface colonies on blood agar, seventy-two hours, 37° C.* Round, convex, with flattened and markedly irregular periphery when observed under low-power objective. Slightly opaque, glistening, gray or pale yellow-white. Easily emulsified. Average 1 mm. in diameter. Subcultured with difficulty.

2. *Growth in serum broth.* Uniformly turbid, later becoming loosely flocculent with relative clearing of the medium after four to six days. Foul odor.

3. *Morphology of organisms, blood agar, surface colonies, 37° C.* Gram-negative, slender, pleomorphic rods and small, coccobacillary rods, varying from 0.5 to 1.5 μ in diameter. Occurs singly and in short chains, components varying from 3 to 10 μ in length; after five to seven days, numerous filmamentous forms, some measuring up to 60 μ in length. Nonspore-forming, nonmotile. Several V and Y forms observed, interpreted as false branching. No true branching observed. In young cultures frequent bipolar rods and long rods with several minute, deeply stained, irregular areas. In older cultures, poorly stained "ghosts" and slightly clubbed forms; occasionally, moderately well-circumscribed, unstained, ovoid areas similar to spores morphologically but failing to stain with spore stains and showing no characteristic resistance to heat.

4. *Physiologic properties.* Obligate anaerobe. Small zone of hemolysis on rabbit blood agar. Acid and gas in dextrose, maltose, and sucrose serum agar.

*Difco Laboratories, Incorporated, Detroit, Mich.

No acid from lactose, glycerol, xylose, and mannitol. No growth in litmus milk in seven days. Serum gelatin not liquefied. Indole produced. No exotoxin demonstrated in four-day cultures.

5. *Pathogenicity for animals.* Inoculation of 0.2 c.c. of a seventy-two-hour culture produced local abscess when introduced subcutaneously in a rabbit. One cubic centimeter of a similar culture inoculated subcutaneously in a rabbit produced irregular, spreading necrosis and death in five to seven days. Five-tenths cubic centimeter, subcutaneously in a guinea pig weighing 250 grams, produced a local abscess which healed spontaneously. Similar amount inoculated intraperitoneally in white mice was fatal in three days.

A bacterium prepared from a known culture of *Bacterium necrophorum,* obtained from Dr. G. M. Dack, was used to hyperimmunize a rabbit. The serum obtained agglutinated the specific antigen in a dilution of 1:640 and organism A in a dilution of 1:320. We believe that these two organisms are taxonomically closely related, perhaps identical. This conclusion is supported by the fact that Orcutt[8] studied several strains of *Bacillus necrophorus* and found that there were different serologic groups.

The nomenclature of this group of organisms is confusing to one who is not familiar with taxonomy of bacteria. Organisms closely similar to, perhaps identical with, the one isolated in this investigation have been cultured from a variety of pathologic lesions in human beings and animals. As previously indicated, the organisms are known in the literature as *Actinomyces necrophorus, Actinomyces pseudonecrophorus, Bacillus funduliformis, Fusiformis necrophorus, Bacterium necrophorum,* and *Bacteroides necrophorus.*

Henthorne, Thompson, and Beaver[9] concluded that *Actinomyces necrophorus* is closely related to *Bacteroides* (or *Bacillus*) *funduliformis* and Dack, Dragstedt, and Heinz[13] have added that their organism, *Bacterium necrophorum,* and *Bacillus funduliformis* are similar and probably identical. It may be, too, that *Actinomyces pseudonecrophorus,* isolated by Harris and Brown,[10] was actually a variant of *Actinomyces necrophorus* and not a different species. The criteria by which they differentiated the forms, namely, the lack of ability to ferment lactose and the failure to hemolyze blood, are probably inadequate to define two species. Both these properties are subject to variation. For example, an organism which fails to hemolyze one type of blood may produce hemolysis of another type. Furthermore, variations between strains of the same species, with respect to ability to decompose carbohydrates, are well recognized.

Organism A, isolated in the present study, is believed by us to be a member of this group, strains of which are known by so many names. Review of the literature reveals, however, that most investigators acknowledge their taxonomic similarity.

If the close relation of these various strains is recognized, in order to clarify the nomenclature, it remains only to select the most proper name for the genus. The organisms are not Actinomyces, which are generally accepted to be gram-positive organisms, producing a branched mycelium which sometimes fragments into conidia or conidia-like bodies. Topley and Wilson recognized a genus, Fusiformis, in which such organisms are classified, with the name *"Fusiformis necrophorus."*[11] However, this genus is not well defined because it includes microaerophilic organisms and some whose reaction to the Gram stain is variable. Furthermore, this generic name is not recognized in

Bergey's Manual of Determinative Bacteriology (1939), which does not attain perfection but, at least, represents the best, most extensive efforts to define the taxonomic relations of bacteria. Bergey's Manual (1939) lists *Actinomyces necrophorus* under the family *Bacteriaceae* in a rather nondescript position as "bacteroides-like organisms fairly well described whose taxonomic relationships are not clear."[12] Likewise, Dack, Dragstedt, and Heinz[13] believed that the strains were typically *Bacteriaceae* and named the organism *"Bacterium necrophorum."* They objected to the generic name "Bacteroides" because it included "Gram-positive and gram-negative species of widely divergent types." However, it should be noted that in the last revision of Bergey's Manual (1939) the genus Bacteroides are: "Motile or nonmotile rods without endospores. Obligate anaerobes. May or may not require enriched culture media. Gram negative." On the other hand the term Bacterium is used to include "nonspore-forming, rod-shaped bacteria whose position in the system of classification is not definitely established," and members of this group may be gram-positive or gram-negative.[12] Therefore, we believe that the most satisfactory name, based on the last edition of Bergey's Manual, is *Bacteroides necrophorus.*

The following characteristics were determined for organism B, which was subsequently identified as *Corynebacterium pyogenes.*

1. *Colonies on blood agar, 37° C.* Minute, almost pin-point colonies observed in twenty-four hours, later enlarge to 2 to 3 mm. Slightly raised, opaque, brown and gray-brown, with convex, dense central area. Difficult to emulsify.

2. *Growth in serum broth.* Turbid with fine, irregular flakes, later forming a granular sediment.

3. *Morphology of organisms, blood agar, 37° C.* Gram-positive, small rods, 0.3 to 0.5 μ wide, up to 2 μ in length, often coccobacillary. Short chains and singly. Stain unevenly but no granules observed with granule stains. Nonspore-forming. Nonmotile.

4. *Physiologic properties.* Facultative anaerobic. Small zone of hemolysis on rabbit blood agar. No growth on plain broth or plain agar. Acid produced in dextrose, maltose, sucrose, lactose, and xylose serum agar. Mannitol not decomposed. Acid and peptonization in serum-litmus milk. Serum gelatin slowly liquefied.

5. *Pathogenicity for animals.* Intravenous injection of 1 c.c. of serum broth culture caused death of a rabbit in four days. Subcutaneous inoculation of 1 c.c. in a rabbit produced a localized abscess which drained spontaneously. Similar treatment of guinea pigs produced small abscess which healed spontaneously.

Corynebacterium pyogenes is known to occur in suppurative lesions of cattle, swine, and other domestic animals and, perhaps, often occurs as a secondary invader in lesions caused by other organisms. Its role in this case is difficult to assess, but on the basis of the relatively few colonies on the plates and the absence or rarity of typical forms in the histologic sections, we believe that *Corynebacterium pyogenes* was a secondary invader, perhaps enhancing conditions for the development of the anaerobe, *Bacteroides necrophorus.* In this respect it is interesting to note that a few subsurface colonies of organisms morphologically similar to *Bacteroides necrophorus,* situated beneath colonies of staphylococci and diphtheroids, were observed on aerobic plates. However, we cannot be positively certain of this because efforts to isolate and

subculture the suspected anaerobes were unsuccessful. The significance of *Bacteroides necrophorus* as the causal agent producing the pulmonary lesions is amplified by the fact that the patient's serum agglutinated the organism in a dilution of 1:160, whereas samples of apparently normal serum failed to produce any clumping of the antigen. Efforts to study serologic reactions with *Corynebacterium pyogenes* were not conclusive owing to auto-agglutination of the antigen.

THE INFECTION IN ANIMALS

Calf diphtheria, or infection of the oral and pharyngeal mucous membranes with *Bacteroides necrophorus*, attracted the attention of such notable bacteriologists as Loeffler, Koch, Theobald Smith, Bang, and others. However, it was Dammann[6] who first observed and recorded the clinical manifestations of this disease, but wrongly concluded that it was caused by *Bacillus diphtheriae*. Loeffler (1884) demonstrated that the causative organism was a gram-negative, pleomorphic bacillus with filamentous forms. He believed this organism to be similar to a bacterium isolated from poxlike lesions in calves three years earlier by Koch. Subsequently, this organism was recovered from lesions in the livers of cattle by Shutz and was associated with ulcerations of the intestines in hog cholera by Bang and Theobald Smith. Schmorl[14] isolated the same organism from necrotic lesions in rabbits in a widespread epizootic. Since this time *Bacteroides necrophorus* has been shown to be the causative agent of numerous common animal diseases, some of which are: necrotic stomatitis of calves, lambs, and pigs; "foot rot" of cattle and sheep; "necrotic quitter" of horses and mules; and necrotizing ulcerations of the intestines in hog cholera. Infections with this organism occur in birds as a form of diphtheria, and have been reported in several species of wild animals including deer, antelope, and apes. An epidemic type of post-partum infection in the vagina and uterus of cows has been reported which is highly fatal. The disease is frequently transmitted to the offspring with resulting omphalophlebitis and the formation of multiple liver abscesses. The disease produced by this organism in horses and mules has a somewhat lower mortality than the infection in cattle.[4]

The pathologic changes produced in the tissues of infected animals are similar to those seen in man. The primary focus of infection is usually in the skin, following injury, or on the mucous membranes, although infection through the gastrointestinal tract undoubtedly occurs. Small abscesses appear followed by liquefaction necrosis and gangrene. The infection may remain localized and in such instances the lesions usually heal in a few weeks. If dissemination occurs it is usually by the blood stream, although lymphatic spread of the infection has been reported. If the inflammatory process at the primary focus of infection is sufficiently severe, thrombophlebitis usually results, which may be followed by embolic spread of the infection, usually to the liver or lungs. Here multiple abscesses occur followed by widespread necrosis of the tissues. Lymphatic dissemination is most commonly seen following a primary focus in the skin, with swelling of the affected part and acute inflammation of the regional lymph nodes. This type of inflammatory reaction and spread is rarely fatal in contrast to blood stream dissemination of the infection which almost invariably results in death.[1-4]

REVIEW OF THE LITERATURE

Schmorl[14] and one of his co-workers each developed a small abscess on one finger after having handled rabbits which had been experimentally infected

with *Bacteroides necrophorus*. Smears of the purulent exudate showed gram-negative, plemorphic bacteria which were considered identical with the organism which had previously been inoculated into the rabbits. The lesions persisted for weeks and healed very slowly. Other instances of acute infections in veterinarians following exposure to animals with necrobacillosis have been reported although in most instances identification of the causative organism was not entirely adequate.[6, 7]

Ellerman[15] reported the case of a 9-month-old infant who developed laryngitis, a necrotizing pharyngitis, and bronchopneumonia. No diphtheria bacilli were recovered on culture and microscopic examination of the uvula showed many threadlike, gram-negative bacteria in the necrotic material adjacent to the viable tissue. The morphologic characteristics of the bacteria and the absence of a positive culture of *Bacillus diphtheriae* as well as the similarity of the lesions to "calf diphtheria" were considered sufficient evidence to report the case as a primary infection with *Bacteroides necrophorus*.

Stemon and Shaw[7] were able to isolate the organism in pure culture from an abscess on the hand of a government meat inspector. The man had scratched his hand on a sheep's tooth while surgically removing a lesion from its lip. The arm became red and swollen and vesicles appeared on the dorsum of the hand followed by foci of necrosis. Healing occurred in three weeks following surgical drainage and the application of hot packs. Van Wering[16] isolated *Bacteroides necrophorus* from material in an abscess on the arm of a man who had been bitten by a cow. There was a bluish discoloration of the forearm followed by lymphangitis and painful enlargement of the axillary lymph nodes. The lesions were not incised and healed slowly with local treatment.

Cunningham[4] (1930) reported two fatal cases with complete bacteriologic and autopsy studies. The first was a 19-year-old girl who developed a sore throat followed by weakness, chills and fever, and pain in the region of the left hip. The sore throat subsequently disappeared, but on the following day there was exacerbation of all symptoms with pain in the left hip on pressure and motion. The temperature ranged between 39 and 41°C. and the white blood cell count rose to 23,000 cells per cubic millimeter. Signs of pulmonary disease appeared and the patient expired on the sixteenth day of illness. At autopsy a large psoas abscess was present with numerous sinuses to the left sacroiliac and iliofemoral joints. Numerous areas of infarction were present in the lung. *Bacteroides necrophorus* was recovered in pure culture from the necrotic material in the infarcts of the lungs and from purulent material in the psoas abscess. One can only speculate as to the course of events in this case but a logical postulation would be that the organism entered the body through the pharyngeal mucous membranes. Dissemination of the infection occurred, which was probably by the blood stream, and localized in the left hip joint. An abscess was formed followed by thrombophlebitis and embolic metastasis to the lungs, which resulted in death. Such a series of events appears to typify infection with this organism. Cunningham's second case presented a somewhat different clinical picture although at autopsy the pathologic findings were consistent with those produced by *Bacteroides necrophorus*. The patient was a 64-year-old clothing cutter who developed a sore throat, followed by chills and fever. The neck became greatly swollen with subcutaneous emphysema over the left side down to the clavicle. Respiratory difficulty developed and despite an emergency tracheotomy the patient succumbed. At autopsy a

retropharyngeal abscess was found which extended into the peritracheal and subcutaneous tissues as well as the superior anterior and posterior mediastinum. There was bronchopneumonia, an acute purulent pleurisy, and irregular foci of acute fibrinous pericarditis. From the purulent material in the tissues of the neck and from the pericardial exudate a gram-negative, pleomorphic, anaerobic coccobacillus was isolated along with several other organisms.

Dack, Heinz, and Dragstedt[17] recovered *Bacteroides necrophorus* from an isolated loop of colon in three human beings with chronic ulcerative colitis and later the same workers recovered this organism from the colons of thirteen of twenty patients. Control cultures on six normal patients were negative. While these investigators do not contend that *Bacteroides necrophorus* is the causative agent of chronic ulcerative colitis, the high number of positive cultures they obtained from patients with this disease suggests that this organism may play some part in its production, in conjunction with other factors as yet unknown. In 1940, Martin[18] described three instances of infection with *Bacteroides necrophorus* with recovery after adequate surgical drainage: one instance of empyema, one of a subdiaphragmatic abscess, and one of an abscess on the back from which *Bacteroides necrophorus* was obtained in pure culture.

Lemierre[19] listed twenty instances of infection with *Bacillus funduliformis* but did not describe the cases in detail. Henthorne, Thompson, and Beaver[9] described four instances of liver abscess in man from which they isolated *Bacteroides funduliformis*. All of these cases, including those of Lemierre, were described as septicemias with metastatic abscesses in the liver.

Chandler and Breaks[20] reported a single instance of osteomyelitis of the neck and head of the femur. Recovery occurred after adequate drainage and sequestrectomy. The organism isolated was a gram-negative, pleomorphic, coccobacillus which on comparison with the strain of *Bacteroides necrophorus* recovered by Dack from patients with chronic ulcerative colitis was considered identical in its biologic and bacteriologic properties.

Meleney[21] listed nine lesions from which he recovered *Bacteroides necrophorus:* (1) A chronic ulcer of the vagina in a little girl, associated with an anaerobic streptococcus. (2) A pelvic abscess associated with an anaerobic streptococcus and a *Staphylococcus albus*. (3) A carbuncle associated with *Staphylococcus aureus*. (4) An appendiceal abscess, associated with a colon bacillus, and an anaerobic streptococcus. (5) A sacrococcygeal cyst, associated with an anaerobic streptococcus. (6) A thyroglossal cyst abscess, in pure culture, without extensive necrosis of tissue. (7) A face infection following a dental abscess. (8) A liver abscess. (9) A postgastrectomy wound infection. In addition to those cited, a careful search in forty cases of chronic ulcerative colitis showed the presence of *Bacteroides necrophorus* in only three instances.[21]

DISCUSSION

Human infection with *Bacteroides necrophorus* usually manifests itself by a primary focus on the skin following trauma or on the mucous membranes, and may either remain localized or be disseminated to other organs or parts of the body through the blood stream. If the infection remains localized it is characterized by large foci of necrosis surrounded by a severe inflammatory reaction consisting of infiltration with numerous polymorphonuclear leucocytes, and occasional lymphocytes and plasma cells. There is an acute arteritis and thrombophlebitis of the vessels immediately adjacent to the foci of necrosis.

The mechanism of dissemination of the infection is usually by the blood stream when infected thrombi break loose and emboli are carried to the other organs, usually the lungs or liver. Dissemination through the lymphatics has been reported with resulting lymphangitis and enlargement of the regional lymph nodes.[16] The pathologic change produced in the distant organs is similar, although usually more extensive, than that seen at the primary focus, namely, the production of metastatic abscesses wherever the infected emboli lodge. As a rule the lesions are characteristic, consisting of large foci of coagulation necrosis surrounded by polymorphonuclear leucocytes, with occasional lymphocytes, plasma cells, and large macrophages being present. In somewhat older foci there are attempts on the part of the host toward healing, with the production of fibrous tissue and the formation of an abscess wall. It is near the periphery of the necrotic tissue that numerous organisms may be found. Their extreme pleomorphism may be well seen in tissue sections. In the necrotic centers of the lesions they appear as small coccobacilli, while near the periphery, in the cellular exudate, they assume a filamentous form. Careful anaerobic cultures of the necrotic material are necessary to isolate the bacteria and care must be taken to scrape the wall of the abscess as relatively few organisms may be found in the center of the necrotic foci.

In the patient reported, the physical examination as well as the observations at the time of autopsy furnish no information regarding a primary focus of infection except the notation that the "pharyngeal tonsils were enlarged and cryptic" and that a "yellowish exudate was present on the left tonsil." There were no lesions observed on the skin and no history of trauma or infection was given. The pharyngeal exudate was not cultured and the neck organs were not removed at the time of autopsy so there is no direct evidence that this lesion was caused by *Bacteroides necrophorus.* However, at the onset of the patient's illness a "sore throat" was one of the first complaints and was present for several days after sulfonamide therapy was begun. The frequency of involvement of the nasopharynx in the previously reported instances of infection with *Bacteroides necrophorus,*[4, 15, 18, 19] plus the fact that that no other focus of infection could be demonstrated would lend support to the assumption that this was the portal of entry of the organism into the body. In this case the explanation of the subsequent development of lung abscess is not difficult. Crowe and Scarff[22] showed that the injection of infected material into the bronchial tree of dogs would produce abscesses of the lung which occurred most frequently in the lower lobe of the right lung. Allen[23] pointed out that pulmonary abscess may be produced in animals by the intrabronchial injection of infected material from human beings if the pus is inoculated into the animal immediately and before cooling has occurred. The development of lung abscess following removal of the tonsils under general anesthesia is well known.[24] Hence, the aspiration of infected material is the most probable mechanism of spread in this instance. The abscess in the lower lobe of the right lung had obviously been present for some time judging from the history and the pathologic findings which consisted of a dense wall of fibrous tissue surrounding the abscess cavity. However, the spread of the infection to the other lobes of the lungs was a relatively recent occurrence as in many foci there were only beginning necrosis and relatively little cellular reaction. The spread undoubtedly occurred through the bronchial tree from the focus in the right lower lobe. The course of events from both the clinical and pathologic viewpoint closely simulated chronic pulmonary tuberculosis. Although there were severe inflammatory re-

actions in the walls of the pulmonary vessels and many of them contained thrombi, no embolic phenomenon occurred and the infectious process remained localized to the lungs, even though the disease had been present and progressive for several months.

The frequency of involvement of the nasopharynx in infections with *Bacteroides necrophorus* suggests that air-borne infections frequently occur and that an outside source or reservoir of the organism should be searched for. Significance should be attached to the environment of individuals with infections with this organism and particularly to contacts with animals, both wild and domesticated, which are known to be frequently infected. The occurrence of infections in veterinarians, meat inspectors, and farmers is significant in that direct contact with animals or meat, or trauma while handling these animals, has resulted in serious infections. The occupation of the individual in the case reported required him to handle and to inspect closely the green hides of both wild and domesticated animals as well as sheep's wool. This may well have been the source of his infection and the upper respiratory tract the portal of entry. Although infections with *Bacteroides necrophorus* have apparently occurred in individuals who have not been in contact with infected animals no specific mention has been made of this in the reported cases. However, the known source of infection in animals should be carefully noted and considered as a hazard to those employed in occupations requiring them to be in contact with animals.

It is probable that human infections with *Bacteroides necrophorus* are much more common than previously supposed and that routine anaerobic cultures as well as careful anaerobic studies in all cases of infections of obscure etiology may show that this type of infection occurs more commonly than previously recognized. Dragstedt, Dack, and Kirsner[25] postulate that *Bacteroides necrophorous* may be a normal inhabitant in the alimentary tract although they have been unable to recover the organism from the colon of normal individuals. This is explained by the extreme difficulty in isolating and cultivating the bacteria on the ordinary media. However, they have been able to recover *Bacteroides necrophorus* from the colons of 70 per cent of the patients they have examined with chronic ulcerative colitis. They state their failure to isolate the organism in the other 30 per cent of cases by the apparent disappearance of the organism from the intestinal tract during periods of temporary recovery or quiescence, at which times the cultures were taken. However, they do not contend that *Bacteroides necrophorus* is the causative agent of chronic ulcerative colitis but that after initial ulceration of the mucosa, presumably by some other agent, there is extension and maintenance of the ulcerated foci by the necrotizing action of this organism. The presence in the patient's serum of agglutinins against the strain of the organism isolated from his own intestinal tract in a higher titer than against other strains of the same species indicates that the specific antigenic properties of the organism were absorbed. Also that the organism persists in isolated loops of colon after other organisms have disappeared is of some significance in the postulation of this organism as an etiologic factor in chronic ulcerative colitis. Although they have failed to recover the organism from the intestinal tract of normal individuals they have succeeded in isolating it from two cases of carcinoma of the rectum, from one case of lymphogranuloma inguinale, and from one case of inflammatory stricture of the rectum. This would lend support to the assumption that *Bacteroides necrophorus* is present in small numbers in the colons of many and that an initial

pathologic change is necessary for the organisms to multiply and hence to be more easily recovered by ordinary methods. However, other workers have been able to isolate the organism in only a few instances and judgment regarding the relationship of *Bacteroides necrophorus* to chronic ulcerative colitis must be reserved. However, their work has shown that extremely careful bacteriologic studies are necessary, in many instances, to isolate this organism and that it may easily be overlooked in the routine examination of cultures.

SUMMARY

A case of lung abscess caused by *Bacteroides necrophorus* is reported. The absence of lesions on the surface of the body plus a history of sore throat and the finding of a purulent exudate on the inflamed tonsils suggests that this is the portal of entry of the organism into the body. The mechanism of the formation of the abscess in the lower lobe of the right lung is probably by the aspiration of infected material. The disease process was confined to the respiratory system and there was an attempt on the part of the host to heal the infection by the formation of a dense wall of fibrous tissue around the abscess cavity. Rupture of the abscess into a bronchus occurred and there was spread of the infection to all other lobes of the lungs. A gram-negative, pleomorphic rod with filamentous and coccobacillary forms was isolated from the pulmonary lesions at the time of autopsy. This organism was an obligate anaerobe, which produced a small zone of hemolysis and acid and gas in dextrose, maltose, and sucrose serum agar. Pathogenicity for rabbits, guinea pigs, and mice was demonstrated. A rabbit was hyperimmunized with a known strain of *Bacterium necrophorus* and the obtained serum agglutinated the recovered organism in dilutions of 1:320 and the specific antigen in dilutions of 1:640. Upon this evidence the organism was classified as *Bacteroides necrophorus*. The nomenclature of this group of organisms is discussed and the name *Bacteroides necrophorus* is given preference on the basis of Bergey's classification.

The patient's occupation as a wool sorter and hide inspector is postulated to be the source of his infection through the upper respiratory tract. The significance of the disease as an occupational hazard to those in close contact with animals is emphasized. Human infections with *Bacteroides necrophorus* are probably more frequent than commonly supposed and careful anaerobic cultures with the utilization of special media and animal inoculation are frequently required to isolate the organism.

CONCLUSIONS

1. A case of lung abscess caused by *Bacteroides necrophorus* is reported.

2. The pathologic changes produced in tissues are quite characteristic.

3. The route of infection was through the upper respiratory tract with the formation of a primary focus in the nasopharynx followed by the subsequent development of a lung abscess.

4. It is postulated that the source of infection in this instance was from the green hides of animals, or from sheep's wool.

5. Infections with this organism constitute an occupational hazard to those required to be in contact with animals.

6. Infections with *Bacteroides necrophorus* are probably more common than previously supposed and careful anaerobic cultures are necessary for the isolation of the organism.

7. The classification and nomenclature of this group of organisms is discussed.

8. The name *Bacteroides necrophorus* is most satisfactory, based on Bergey's classification.

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THE SIGNIFICANCE OF FLUID IN THE PLEURAL SPACE

A Study of 274 Cases

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IN MEDICAL terminology a variety of terms has been used to indicate that fluid is present in the pleural space. Use of these terms presupposes knowledge of the etiologic factors involved in production of pleural fluid, which may be serous, hemorrhagic, or chylous in nature.

In the condition known as hydrothorax, which is most commonly the result of congestive heart failure, nephritis with edema, cirrhosis of the liver, and occasionally mediastinal tumors, the fluid is clear and serous and of low specific gravity. It is called a transudate. Mechanical factors such as increased intracapillary pressure and increased capillary permeability are involved in instances of cardiac failure, cirrhosis of the liver, and obstructions to the large veins of the pulmonary circulation. Changes in osmotic pressure are responsible for the hydrothorax of the nephrotic syndrome.

The term pleurisy with effusion is applied to collections of fluid in the pleural space which result from inflammation of the pleura. Pleuritis may be caused by the spread of inflammatory processes in the pulmonary parenchyma to the pleura or by obstruction to a bronchus or artery supplying a pulmonary segment. The fluid in a pleural effusion is considered to be an exudate rather than a transudate. It is serous and may vary greatly in color and degree of turbidity. Its specific gravity exceeds 1.012. When a pleural effusion becomes infected, empyema is said to be present.

When fluid in the pleural space contains enough red blood cells to produce a pink or red color the condition is known as hemorrhagic pleural effusion. Approximately 5,000 to 6,000 red blood cells per cubic millimeter are required to produce a red tint to the fluid. A smaller number of cells rarely produces any change in the color of the effusion. Changed hemoglobin usually imparts a brown or amber color to the fluid. If pure blood is present in the pleural space, the condition is called hemothorax.

Disturbances in the lymphatic circulation may result in a condition called chylothorax, in which milky fluid containing an excess of fat globules accumulates in the pleural space. Chylous fluid usually forms a creamy top layer on standing.

The differential diagnosis of fluid in the pleural space may pose a difficult problem and in many instances its cause can be determined only by aspiration and examination of the fluid. Our purpose in this paper is to discuss the differential diagnosis of this condition and to present a statistical survey of a group of cases encountered at the Mayo Clinic. We have, therefore, reviewed 444 cases in which fluid was present in the pleural space and in which diagnostic thoracentesis

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was performed. If, in any case, pleural effusion developed as a postoperative complication or as the result of trauma, the case was excluded from this investigation.

The group of 444 cases includes 170 cases (38 per cent) in which a diagnosis of the underlying disease was not established. Of this group of 170 cases there were 58 in which a tentative diagnosis of tuberculosis never was confirmed and 46 cases in which metastatic carcinoma of the pleura was suspected; even less definite diagnostic impressions were secured in the remaining 66 cases. Although these 170 cases were interesting because they presented a difficult problem in diagnosis, we decided to limit the present statistical study to the 274 cases in which the cause of the pleural effusion was established.

ETIOLOGY IN GENERAL

The etiologic factors responsible for production of pleural fluid in the 274 cases are listed in Table I.

Carcinoma.—The high incidence of carcinoma in contrast to inflammatory lesions, such as pneumonia and tuberculosis, is explained by the type of cases encountered at the Mayo Clinic and may be somewhat out of proportion to the experience of others. On addition of the figures for carcinoma and lymphoblastoma it is found that in 61 per cent of the series the fluid was secondary to a malignant lesion.

TABLE I

ETIOLOGY OF PLEURAL FLUID IN 274 CASES

ETIOLOGY	CASES	PER CENT
Carcinoma	141	51
Congestive failure	42	15
Lymphoblastoma	28	10
Pneumonia	24	9
Tuberculosis	16	6
Cirrhosis of the liver	8	3
Chronic nephritis with nephrosis	7	3
Miscellaneous conditions	8	3

As would be expected, the highest incidence of pleural effusion occurred in cases of intrathoracic tumor and in carcinoma of the breast (Table II). A review of 448 cases of bronchiogenic carcinoma by Moersch and one of us (W. S. T.)[1] revealed that in 15 per cent of cases there was a pleural effusion large enough to be diagnosed clinically.

TABLE II

PLEURAL EFFUSION ASSOCIATED WITH PRIMARY NEOPLASM IN 141 CASES

SITE	CASES	PER CENT
Intrathoracic	51	36
Bronchiogenic carcinoma	47	
Mediastinal carcinoma	4	
Breast	42	30
Ovary	12	8
Kidney	6	4
Stomach	5	4
Colon and rectum	4	3
Lower part of urinary tract	4	3
Esophagus	1	1
Thyroid	1	1
Jejunum	1	1
Primary site not established		
Carcinomatous	12	8
Melanocarcinomatous	2	1

Malignant cells were found in the aspirated fluid in 42 of the 141 cases of carcinoma (30 per cent), as shown in Table III.* There were two cases of lymphoblastoma in which malignant cells were found in the fluid.

TABLE III

EXAMINATION OF PLEURAL FLUID IN 141 PROVED CASES OF CARCINOMA

	CASES		PER CENT OF CASES OF CARCINOMA		OF TOTAL (274)
Hemorrhagic fluid	59		42		22
Positive for malignant cells		13		22*	
Negative for malignant cells		46		78*	
Serous fluid	82		58		30
Positive for malignant cells		29		35†	
Negative for malignant cells		53		65†	
Total, malignant cells found	42		30		

*Per cent of fifty-nine cases in group.
†Per cent of eighty-two cases in group.

Congestive Failure.—In the forty-two cases of congestive failure, the effusion was on the right side in twenty-eight cases and bilateral in one case. There were two cases of chronic constrictive pericarditis and two cases of acute pericarditis.

Tuberculosis.—The low incidence of tuberculosis is partially explained by the fact that all patients who had received collapse therapy were excluded. Tuberculous effusions sometimes are found in patients who otherwise have little evidence of the disease. For this reason the diagnosis may be difficult. In only four of our sixteen cases was there a demonstrable lesion in the parenchyma of the lung. In four cases the sputum was positive for *Mycobacterium tuberculosis.* In three cases the organism was isolated on culture of the fluid. After injection of the fluid into guinea pigs *Mycobacterium tuberculosis* was recovered in nine cases.

The miscellaneous group included two cases of bronchiectasis and one case, respectively, of actinomycosis, echinococcus disease, amebiasis, lupus erythematosus, osteomyelitis of the spinal column with empyema, and perforated peptic ulcer with subphrenic abscess and empyema.

ETIOLOGY ACCORDING TO TYPE OF FLUID

Serous Fluid.—The etiology of serous effusion is shown in Table IV.

Hemorrhagic Fluid.—Berliner[3] reviewed 120 cases of hemorrhagic pleural effusion and found that in seventy-eight cases (65 per cent) the effusion was caused by a malignant neoplasm. His experience indicated that frank hemorrhage into the pleural space from a tumor was not unusual. Berliner concluded that the finding of pure blood in the pleural space limited the differential diagnosis to two condi-

*In studying serous effusion for malignant cells, the technique described by McDonald and Broders[2] was used. From 20 to 40 c.c. of the fluid were centrifuged for fifteen minutes at approximately 1,800 revolutions per minute. The fluid was centrifuged immediately after its removal, before the formation of a clot. The centrifugate was smeared quickly on clean glass slides and was allowed to dry in air. The slides were immersed in a solution of formaldehyde, U.S.P. (dilution 1:10), for twelve hours and the smears then were stained with hematoxylin and eosin, carried through the alcohols, carbolxylene, and xylene and mounted in Canada balsam. McDonald and Broders found that the diagnosis of malignant cells is most readily made by finding large cells with large nuclei and nucleoli. Mitotic figures, although difficult to find, were of aid in making the diagnosis. It was the experience of McDonald and Broders that smears made from the sediments of fluids are as helpful in studying cellular detail as paraffin sections. Clumped cells and cells with eccentric nuclei were of little value in making a diagnosis. The addition of an anticoagulant preparation to the fluid will prevent clotting and will facilitate the examination of hemorrhagic fluid.

TABLE IV

ETIOLOGY OF SEROUS PLEURAL EFFUSION IN 193 CASES (70 PER CENT OF 274)

ETIOLOGY	CASES	PER CENT
Carcinoma	82	42
Congestive failure	34	18
Pneumonia	23	12
Lymphoblastoma	18	9
Tuberculosis	15	8
Chronic nephritis with nephrosis	7	4
Cirrhosis	6	3
Miscellaneous	8	4

tions, namely, spontaneous hemopneumothorax and neoplasm of the pleura. In his series the frequency with which tumor cells were found in the fluid was the same in serous as in hemorrhagic effusion. There were only eight cases of tuberculosis in Berliner's group. His experience is in contrast to the opinion of Norris and Landis[4] that tuberculosis is the commonest cause of hemorrhagic pleural effusion. The results of our study, as shown in Table V, agree with Berliner's finding that hemorrhagic pleural effusion of tuberculous origin is not of common occurrence.

TABLE V

ETIOLOGY OF HEMORRHAGIC PLEURAL EFFUSION IN 81 CASES (30 PER CENT OF 274)

ETIOLOGY	CASES	PER CENT
Carcinoma	59	73
Lymphoblastoma	10	12
Congestive failure	8	10
Cirrhosis of the liver	2	2
Pneumonia	1	1
Tuberculosis	1	1

In our series there were eighty-one cases (30 per cent of 274) in which the effusion was hemorrhagic (Table V). It is interesting that in 85 per cent of cases of hemorrhagic effusion the underlying disease was a malignant process, either carcinoma or lymphoblastoma. In an additional 10 per cent, the cause was congestive failure. This fact is of clinical significance because if congestive failure can be eliminated as a cause of bloody effusion in a specific case there is a 95 per cent chance that a malignant process, either carcinoma or lymphoblastoma, is present. It is also interesting to note that in almost one-half of the cases of carcinoma (42 per cent) there was hemorrhagic effusion.

Of the eight cases of congestive failure in which the fluid was hemorrhagic, in five pulmonary embolus was a complicating condition. Hemorrhagic effusion may be the only clinical manifestation of pulmonary infarction; consequently, in the other three cases also pulmonary embolus, with infarction, may have been present.

The occurrence of bloody pleural fluid in the presence of cirrhosis of the liver was considered to be extremely unusual by Christian,[5] who reported such a case in 1937. There was one such case in Berliner's series. In two of our eight cases of cirrhosis bloody pleural effusion was found.

Chylous Fluid.—A report of our experience with chylothorax recently was published by Wilson and one of us (A. M. O.).[6] This condition is frequently difficult to recognize unless the pleural fluid is carefully examined. Oil droplets often can be recognized if the fluid

is dropped on a glass slide. The addition of alkali and ether results in clearing of the fluid. The fat droplets readily can be demonstrated by staining with sudan III. Chemical examination of the fluid discloses that the total fat content varies from 0.4 to 4 per cent. If cases of chylothorax caused by trauma to the thoracic duct are excluded, neoplastic disease probably is the commonest cause of accumulation of chylous fluid.

COMMENT

The presence of fluid in the pleural space is almost always indicative of serious organic disease. It is doubtful whether pleural effusion is ever a primary disease. In our series of 444 cases of fluid in the pleural cavity a definite diagnosis was not made in 170 instances. Yet there was clinical evidence to favor a diagnosis of either tuberculosis or neoplastic disease in 104 of these cases. In the remaining sixty-six cases a diagnosis might have been made if there had been an opportunity for observation or further studies of the pleural fluid.

It is important to emphasize the necessity for careful examination of aspirated pleural fluid. The gross characteristics should be accurately recorded and the specific gravity and number of cells should be determined. A search for neoplastic cells, either by the method previously described or by the paraffin section method, should be made. Bacteriologic study should include cultures on suitable media and frequently also inoculation of guinea pigs. When the presence of chylothorax is suspected, the fluid should be stained with sudan III, shaken with ether, and chemically analyzed for fat.

In a considerable number of cases it is difficult to establish an exact diagnosis. In most instances it is wise to suspect tuberculosis and to treat the patient accordingly.

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CYSTIC LYMPHANGIOMA OF THE MEDIASTINUM

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INCLUDED among the benign tumors of the mediastinum are the true cysts. These have been classified: epidermoid, bronchiogenic, gastrogenic, lymphangiomatous, venous, pericardial, pleural, mixed (dermoid), and undetermined cysts.

The following case of cystic lymphangioma of the mediastinum is added to the literature because of (1) the rarity of the lesion, (2) the clinical and radiographic problems in diagnosis, and (3) the surgical result obtained for the patient.

REPORT OF CASE

History.—V. C. (File No. 185446), a 59-year-old white man, a barber, was admitted to the Edward J. Meyer Memorial Hospital, Nov. 1, 1943. He was discharged Nov. 27, 1943.

Except for a chronic bronchitis with nonproductive cough which he had had for many years, the patient felt well until five weeks before entry to the hospital, when he had a gastric upset. Fearful of a carcinoma of the esophagus, the patient sought a medical examination. No relevant physical abnormalities were noted. Roentgen-ray studies revealed a dense, rounded, nonpulsating mass in the upper right hemithorax between the trachea and esophagus which were deviated slightly to the left (Fig. 1). There was no intrinsic lesion of the esophagus. The mediastinal mass showed no response to a test dose of 975 r. Laboratory data were not remarkable. On bronchoscopic examination the trachea and bronchi were clear. An electrocardiogram disclosed slight right axis deviation.

The clinical impression was benign tumor of the mediastinum, neurofibroma(?); cyst(?). The patient consented to an exploratory thoracotomy.

Operation (Nov. 13, 1943).—Intratracheal gas-ether anesthesia. An incision was carried from three inches lateral to the first dorsal spine on the right to a point opposite the seventh dorsal spine, and then along the seventh rib to the midscapular line. The right scapula was mobilized and pulled upward. A segment of the fifth rib was taken out and the thorax was opened through the bed of this rib. The apex of the right lung was mobilized by cutting pleural adhesions. There was a marked bulge of the mediastinal pleura into the right pleural cavity. Over this bulge ran the azygous vein. The mediastinal pleura was incised. A soft, grapefruit-sized cyst occupied the space between trachea, esophagus, and mediastinal pleura. It extended superiorly to the sternal notch. The cyst was mobilized from the surrounding tissue, including the azygous vein, and removed. Bleeding was moderate in amount. The mediastinum was closed with running sutures of plain catgut. The thorax was closed with interrupted chromic sutures and the skin, with interrupted silk sutures.

Pathologic Description:—

Macroscopic: The specimen was a grapefruit-sized cyst about 10 cm. in diameter. The cyst was apparently well encapsulated. The surface showed evidences of adhesions. In places it was covered by fatty tissue. The surface was not altogether smooth; in areas it had small protuberances. The wall was 0.15 cm. thick. The content was a thin, watery yellow and yellow-brown fluid. The inner surface of the cyst was distinctly trabeculated. Separate small cysts were found in the wall of the large cyst (Fig. 2).

Microscopic: The lining of the large cyst was for the most part absent. In certain areas it was preserved in the form of flat cells with diffusely dark-staining nuclei. The inner surface showed papillary elevations on the basis of collections of smooth muscle fibers or lymphocytes. The wall varied in thickness. It contained a good amount of smooth muscle, especially in the inner third. Otherwise the wall was composed of compact and edematous

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connective tissue with thin, wavy spindle-shaped nuclei. Scattered through the wall were focal and diffuse infiltrations of lymphocytes. Neutrophiles, plasma cells, and eosinophiles were also seen. In places the focal collections of lymphocytes assumed the structure of lymph follicles. Some of these had reactive centers. In certain sections the lymphocytic infiltrations and lymph follicles were most abundant in the inner zone of the wall; in other sections, the outer third of the wall was predominantly involved. Lymph follicles revealed hemosiderosis and lipoid resorption in foamy cells. Hemosiderosis was also proved in the mural connective tissue of the cyst. The wall showed blood vessels with thin or slightly thickened walls. Frequently the vessels were dilated. There was perivascular round cell infiltration. In various areas of the cyst wall were present, singly or in groups, small to large spaces lined by flat cells and often filled with pink-staining rather homogenous fluid. In the fluid floated round cells, mononuclear cells, and an occasional eosinophile. The outer layer of the cyst showed varying amounts of fat tissue (Fig. 3).

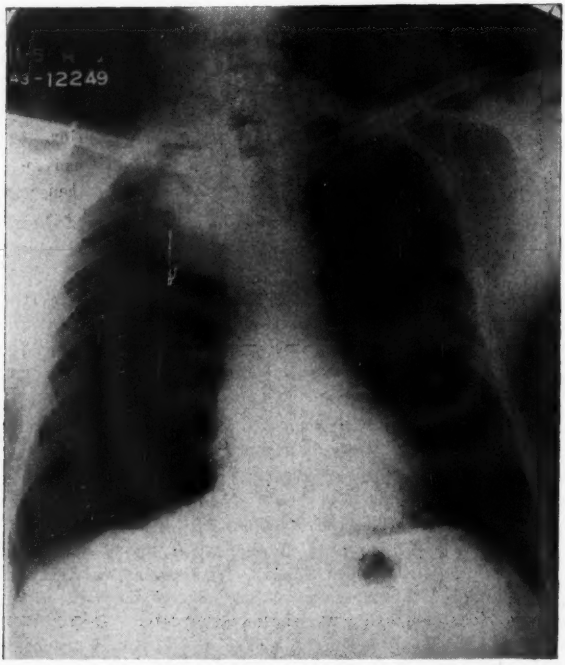


Fig. 1.—Preoperative roentgenogram showing intrathoracic mass.

The pathologic diagnosis was cavernous cystic lymphangioma.

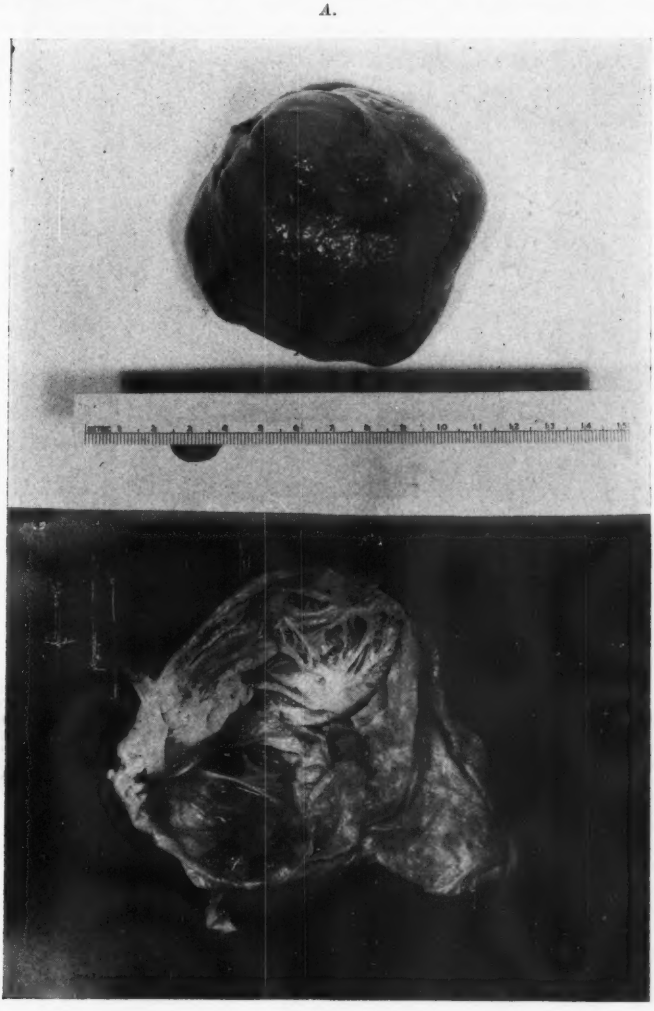
The immediate postoperative convalescence was uneventful except for persistence of some mediastinal broadening on x-ray film and the development of hoarseness. Subsequently the right vocal cord was found to be paralyzed; the mediastinum was of normal width (Fig. 4).

COMMENT

From a diagnostic standpoint, the case described was of challenging interest. The patient really came to a physician for cancerophobia. The mediastinal lesion was a surprising discovery on x-ray examination of the chest. As far as one could recognize, the mediastinal lesion did not satisfactorily explain recent symptoms. Whether the so-called bronchitis with nonproductive cough of many years' duration was related to the mediastinal lesion had to be considered. With the lack of definitely linked symptoms, with the negative report from the bronchoscopist, and with the failure of the mass to progress in size on

repeated roentgen-ray examinations or to respond to a therapeutic dose of x-ray, the mediastinal lesion was thought to be most likely a benign tumor, neurofibroma (?) or cyst (?).

Exploratory thoracotomy was advised for conclusive diagnosis and for possible surgical treatment. At operation, when the mediastinal lesion was found to be cystic, the thin watery content spoke against epidermoid, bronchiogenic,



A.

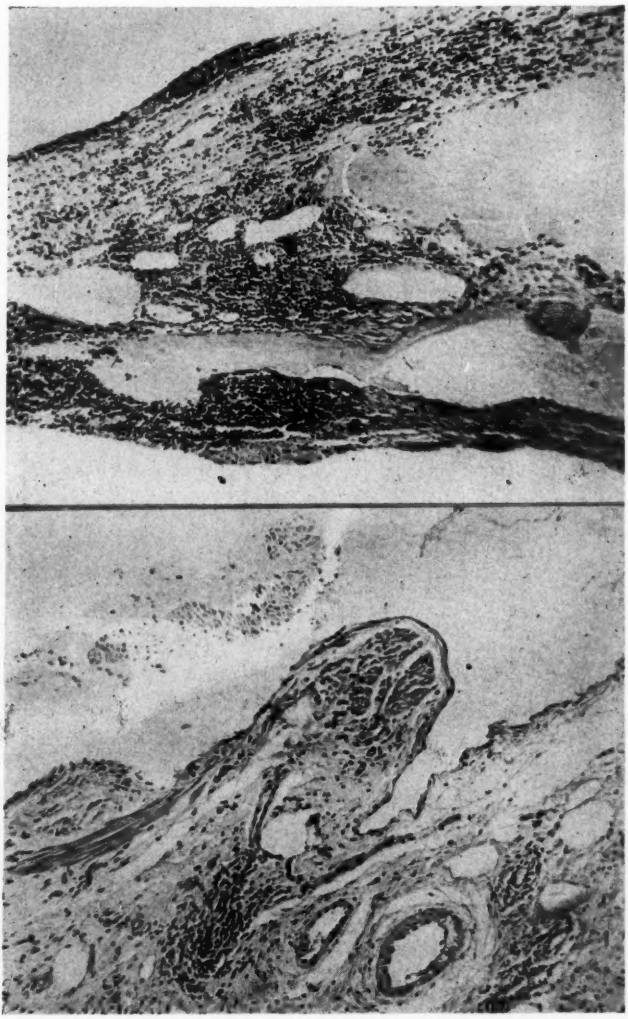
B.

Fig. 2.—*A*, External view of cyst, *B*, internal view of cyst.

gastrogenic, or venous cyst. Grossly a lesion of lymphangiomatous or pleural origin was suspected. The microscopic evidences—flat lining, pink-staining fluid content with round cells and mononuclear cells, multilocularity, smooth muscle, and lymphocytic collections in wall—proved the diagnosis of cavernous cystic lymphangioma.

Several points connected with the operation and postoperative course in our case were of practical interest. For a lymphangioma, the cyst was mobil-

ized and enucleated with relative ease. The hoarseness developed probably on the basis of damage to the recurrent laryngeal nerve. The widening of the mediastinum, demonstrated on x-ray film shortly after removal of the cyst, which later disappeared (Fig. 4), was thought to be due to accumulation of blood.



A.

B.

Fig. 3.—*A*, Wall of cyst showing cavernous spaces and lymphocytic infiltration, *B*, inner part of wall of cyst showing smooth muscle fibers.

Primary lymphangioma is one of the rarest cysts of the mediastinum. The *Quarterly Cumulative Index Medicus* lists only one American report under the heading "mediastinum-lymphangioma." In 1936, Skinner and Hobbs[1] described an adherent, multilocular, cystic lymphangioma located chiefly in the right pleural cavity but apparently arising from the mediastinum. The patient was a 7-year-old boy who complained of shortness of breath, nonproductive

cough, orthopnea, and tightness of chest, among other symptoms. The lesion was removed in two operations through an anterolateral incision. There was no recurrence of the tumor one and one-half years following the extirpation. Skinner and Hobbs pointed out that the possibility of cystic lymphangioma of the mediastinum had been mentioned by Ewing, Nasse, Lilienthal, and Sauerbruch.

Single cases of cysts specifically designated as primary mediastinal-intrathoracic lymphangiomas have been reported in the foreign literature by Seidel[2] (thymus), Eigler,[3] Lenkeit,[4] Dufour and Mourrut,[5] Eliaschewitsch,[6] Michaelis,[7] and Bumin.[8] Other cysts recorded in which histologic examination was not made or in which the lining was not preserved for exact microscopic diagnosis possibly belong, from available pathologic description, to the lymphangiomatous group. In 1939, Stout[9] referred to "lymphangioma" in discussing Foot's

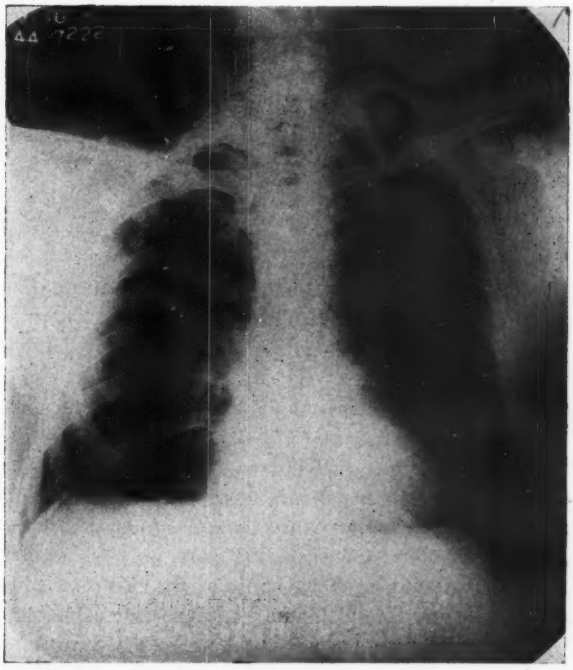


Fig. 4.—Postoperative roentgenogram showing mediastinum of normal width.

paper on mediastinal tumors. According to Lambert,[10] cystic lymphangioma must be differentiated pathologically from celomic, that is pericardial and pleural, cysts. On the basis of Lambert's beliefs certain cystic lymphangiomas reported might have to be considered celomic in origin. In an individual case, however, absolute differentiation between lymphangiomatous cyst and celomic cyst, solely on the structure of the lining, may be difficult. In our specimen, the presence of cavernous spaces, smooth muscle, and lymphatic architecture in the wall denoted a lymphangiomatous character. Primary mediastinal lymphangioma should be classified separately from cervicomediastinal lymphangioma.

We are indebted to Dr. William F. Jacobs, Chief Pathologist, Edward J. Meyer Memorial Hospital, for criticism.

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NONTUBERCULOUS LUNG ABSCESSES IN CHILDREN

SURVEY OF SIXTY-FOUR CASES

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NEW ORLEANS, LA.

THERE have been numerous reports of lung abscesses in total hospital admissions, based on a study of all age groups, but relatively few of the reports are confined to a study of the disease in children. Hence, our attention was drawn to this phase of the subject.

According to Griffith, nontuberculous abscess of the lung of any considerable size is a very exceptional occurrence in early life. Smith surmised that "pulmonary abscess is not diagnosed as frequently in children as in adults and is probably due to the fact that it occurs less commonly and is more difficult to differentiate from other pulmonary infections." Among 2,250 cases of lung abscess collected by him from American literature, only 59 were in infants and children. Holt and Howland, in 1928, wrote of the rarity of lung abscesses in children. Struthers reported, in 1926, that only one case of acute pyogenic lung abscess in an infant under 1 year of age had been reported in the last ten years. Based on the assumption of the rarity of lung abscesses in children, and particularly in infants, Struthers felt that the case of an infant aged 24 days, who had a lung abscess, warranted a report.

However, the assumption that lung abscesses in children are a rarity is not substantiated by this study. Of the 417 cases of lung abscesses which are being reported upon, 64 cases, or 10.5 per cent, occurred in children of 13 years or younger. Of these 64 cases, 19, or 29 per cent, were in children of 1 year of age or younger, and 9, or 14.1 per cent, of these were autopsied with acute lung abscesses. Consequently, the hypothesis stated by Griffith of the rarity of lung abscesses in children and the one stated by Struthers were disproved by these cases which occurred in children under 13 years, indeed, in infants of 1 year and younger; the autopsied cases were further conclusive evidence. Substantiation of these findings might be sought in a study made by Graham. He

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found that of 218 patients with pulmonary suppuration, 40, or 18.3 per cent, were children under 12 years of age. Debre and associates concluded that lung abscesses were rather frequent in children, after having observed 17 cases between January, 1934, and July, 1936, in children whose ages ranged from 9 months to 13 years.

This report will include all of the cases of lung abscess occurring in individuals of 13 years of age or less, during the ten-year period 1931 to 1941, at Charity Hospital in New Orleans. During this period there were 417 cases of abscesses of the lungs. Sixty-four, or 10.5 per cent, of these occurred in patients whose age groups ranged from 0 to 13 years. The results of the cases were taken from discharge records as the patients left the wards, and are not concerned with the progress or regressions after leaving. Of the 64 patients, 42, or 65.6 per cent, were males and 22, or 34.4 per cent, were females. There were 51 white patients, or 79.7 per cent, and 13 Negro patients, or 20.3 per cent. Of the entire group 1 patient was cured (1.5 per cent), 24 patients improved (37.5 per cent), 13 were unimproved (20.3 per cent), and 26 died (40.6 per cent).

In Table I age groups are recorded in relation to outcome and mortality rates. Owing to the small number of cases in each age group, any definite conclusions as to whether age is a significant factor in mortality are unjustifiable. The incidence of lung abscesses in relation to age groups, excluding the first age group, is of no significance because of the irregular distribution and the relatively small numbers. However, the first group of 0 to 1 year of age comprises approximately a little less than one-fourth of the cases; therefore, a 92.9 per cent mortality in that group might be significant.

The outcome in relation to race and sex is indicated in Table II. From this table it may be seen that in the group of cases there was a much higher incidence of lung abscesses in the white patients. Fifty-one, or 79.6 per cent, were white. Also, it can be seen that the incidence of the disease was greater in males than in females. There were 42 males (65.6 per cent) and 22 females (34.3 per cent). It is not feasible to define the causation of this. Flick found that in 172 cases, 108 (62.8 per cent) involved males.

TABLE I. AGE GROUPS IN RELATION TO OUTCOME AND MORTALITY RATE

A. G.	C.	I.	U.	D.	T.	M. R. (%)
0-1	0	1	0	13	14	93.1
2	0	0	0	1	1	100.0
3	0	0	2	1	3	50.0
4	0	1	0	4	5	80.0
5	0	3	0	1	4	25.0
6	1	2	0	0	3	0.0
7	0	3	1	1	5	20.0
8	0	0	0	1	1	100.0
9	0	5	3	0	8	0.0
10	0	2	3	0	5	0.0
11	0	2	2	2	6	33.3
12	0	0	1	0	1	0.0
13	0	2	2	0	4	0.0
Total	1	21	14	24	60	
Percentages	1.5%	35.0%	23.4%	40.0%		

A. G., age group
C., cured
I., improved
U., unimproved
D., died
T., total
M. R., mortality rate

TABLE II. OUTCOME IN RELATION TO RACE AND SEX

	WHITE		NEGRO	
	MALE	FEMALE	MALE	FEMALE
C.	1	0	0	0
I.	13	8	0	1
U.	11	2	1	1
D.	13	3	3	7

Some of the factors responsible for the etiology of the abscesses can be found in the first column of Table III. The other columns indicate whether the patient was cured, improved, or unimproved, or whether he died.

In an earlier paper, a general consideration of lung abscesses at Charity Hospital including all age groups, the conditions preceding lung abscesses were found to be quite different from those in the present study limited to children. In the former survey it was found that in 13 per cent of the total cases pneumonia preceded the disease, and in 8 per cent tonsillectomy preceded the disease. These figures for children, however, exhibit 32.2 per cent as having had preceding pneumonia, and 19.3 per cent as having had preceding tonsillectomy.

TABLE III.

ETIOLOGY	OUTCOME					
	C.	I.	U.	D.	T.	%
Pneumonia	0	4	1	5	10	32.2
Tonsillectomy	0	3	2	1	6	12.3
Aspiration of mucus	0	0	0	1	1	3.2
Otitis media	0	1	0	1	2	6.4
Whooping cough	0	1	0	1	2	6.4
Fractured skull	0	0	1	0	1	3.2
Aspiration of peanut	0	0	3	2	5	16.1
Diphtheria	0	1	0	0	1	3.2
Furunculosis	0	0	0	1	1	3.2
Appendectomy	0	2	0	0	2	6.4

In an article by De Verges it is stated that the most common cause of lung abscess is previous surgery. Of a combined series of 2,548 cases, 657 (26 per cent) had an operative procedure as a predisposing cause. He lists pneumonia as the next most common contributing factor. This is not in keeping with the findings herein tabulated, nor with those of Smith.

In a report by Debre it is stated that the abscess never complicated pneumonia. In the current study there were 10 cases (32.2 per cent) in which pneumonia preceded lung abscesses.

Ochsner and Nesbit pointed out that lung abscesses following tonsillectomy have been increasing since Richardson's first description of pulmonary abscess as a complication of tonsillectomy in 1912. According to Flick, in a report on 172 cases in which the age range was 1.5 to 66 years, 70 per cent of the lung abscesses followed surgery, and 25 per cent followed acute infections of the respiratory tract.

According to Smith, pulmonary abscesses can be divided on the basis of etiology into three groups: (1) bacterial abscesses, (2) fusospirochetal abscesses, and (3) fungous abscesses. The source of the mixture of organisms which is responsible for the fusospirochetal type of abscess is generally the gums or the tonsils of the patient. It is Smith's opinion that there are four possible routes by which the infecting material may reach the lungs: It may be introduced directly by a penetrating wound; it may drain in through the lymphatics; it may enter through the blood stream as an embolus; or it may be aspired.

From Table III it would seem that improvement is much more likely to occur in cases where the factors responsible for the etiology were tonsillectomy

and abdominal surgery. However, I believe that it would be rather difficult to point out, in such a small group, any one outstanding cause or causes of lung abscesses. In fact, the present clinical study of lung abscesses, supported by the literature already written on the subject, leads one to believe that it is not possible to draw definite conclusions as to the etiology of the disease. Mathews states that children have become more subject to pulmonary suppuration in recent years, and he names "wholesale tonsillectomy" as the chief cause. This assertion does not seem justifiable in view of the fact that children's diseases and the aspiration of foreign bodies have been present since time immemorial.

There were 42 (65.6 per cent) incidents of singular lung abscesses, 16 (25 per cent) of bilateral or multiple abscesses. In 6 (9.4 per cent) of the cases, only the side involved was given, without an attempt to localize the lesion to a given lobe. Of the 42 patients having singular lung abscesses, the outcome is demonstrated in Table IV.

In this series there is a definite predominance of abscesses on the right side, as there were 27 (64.3 per cent) on the right side and 15 (33.7 per cent) on the left side, which is approximately a 2:1 ratio. This is quite contrary to the statement by Debre that abscesses occur with equal frequency on either side.

Not only were lung abscesses more frequent on the right side, but the lower lobe was involved more frequently than the upper lobe. Sixty-three per cent of the right lung abscesses occurred in the lower lobe. Of all the cases, 61.9 per cent occurred in the lower lobes. This is in keeping with a study made by Mathews, while Flick found that the upper lobe was more frequently involved. Of those patients, 33 per cent having right lobe infection died, 25 per cent of those with midlobe infection died, and 23.6 per cent of those with infection in the lower right lobe died.

TABLE IV. OUTCOME OF SINGULAR LUNG ABSCESSES

SIDE	LOCATION	C.	I.	U.	D.	T.	%
Right	Upper	0	4	0	2	6	14.3
	Mid	0	2	1	1	4	9.5
	Lower	0	7	6	4	17	40.5
Subtotal		0	13	7	7	27	64.3
Left	Upper	0	3	1	2	6	14.3
	Lower	0	5	2	2	9	21.4
Subtotal		0	8	3	4	15	35.7
Total		0	21	10	11	42	
Percentages		0	50	23.8	26.1		

Even though the number of cases, 42, is insufficient for drawing definite conclusions, it is evident that chances of survival were greater if the infection occurred in the lower lobe. This is further substantiated by the mass statistics from Charity Hospital.

In Table IV it can be seen that there were 50 per cent of the patients improved and a mortality rate of 26.1 per cent in singular lung abscesses.

The occurrence of lung abscesses on the right side is approximately twice that on left side. However, the mortality rate is approximately the same: 25.8 per cent of those with lung abscesses of the right side died and 26.6 per cent of those with abscesses of the left side died.

There was a mortality rate of 87.3 per cent in bilateral or multiple abscesses. Of the 16 patients with multiple lung abscesses, 14 died. This is in keeping with the mortality rate of 68.7 per cent in the total statistical report from this institution.

Debre stated that he did not believe that lung abscesses tend to become chronic in children, and asserted that fatality therefrom is very low. In the course of the present study it was found that there were 8 cases in which hospitalization was over fifty days, and one of those patients remained hospitalized 119 days. The mortality rate was not low, amounting to 40.6 per cent.

The report by Debre in which only 3 patients (17.7 per cent) had an accompanying empyema may be contrasted with this study in which there were 14 (21.9 per cent) with empyema, of which there were 11 deaths (78.5 per cent). These figures do not tally with the report by Debre in which it is stated that empyema does not seem to "modify the favorable course of the abscess."

In Table V is indicated the outcome of patients in respect to the number of weeks ill prior to hospitalization. There were 51 patients in whose histories was stated the length of illness prior to hospitalization. Twenty-three (45.1 per cent) of the patients entered the hospital during the first week of their illness. Of the 23 patients, 10 died (43.5 per cent). Twenty-eight (54.9 per cent) of them entered the hospital some time after the second week of their illness. Of this number, 7 (25 per cent) died. Ten patients (19.6 per cent) of the entire group who entered the hospital during the first week of their illness died, while 25.5 per cent were either improved, cured, or unimproved. Of the patients, 6.1 per cent died who entered the hospital during the ninth week of their illness or later, while 9.7 per cent of the patients who entered the hospital that late

TABLE V. OUTCOME OF PATIENTS IN RESPECT TO THE NUMBER OF WEEKS ILL PRIOR TO HOSPITALIZATION

OUTCOME / WEEKS	7	14	21	28	35	42	49	56	63 AND OVER
I.	8	2	2	1	0	0	0	0	4
U.	5	4	3	1	0	0	0	1	1
D.	10	2	2	1	0	0	0	0	3

in their illness were either cured, improved, or unimproved. As can be noted from Table V, the percentages grow smaller as the duration of illness progresses.

From this it would appear that those patients who entered the hospital during the first week either were more acutely ill or the disease was more virulent. It would seem that in those patients who entered thereafter the disease was either less virulent or tended to be chronic in nature. For this, it can be shown that 68.9 per cent of the patients entering the hospital after the first week survived. These figures are definitely contrary to those put forth by Sweet and many others who believed that if the disease were treated early enough chances of survival were greater. The mortality rate of patients entering the hospital during the first week of their illness is 43.5 per cent, as stated previously. Also, more than one-half of all the deaths in the group took place in those who entered during the first week of their illness. Of all the deaths, 17.6 per cent occurred in those patients who did not enter until after the ninth week, or later, of their illness.

On the other hand, of the 32 patients who were either improved, unimproved, or cured, 40.5 per cent entered the hospital during the first week of their illness, while 15.7 per cent did not enter until the ninth week or later.

Total mortality rate was 40.6 per cent. This is in keeping with the rates found in other studies. In a study by Brunn, the mortality rate of lung abscess was found to be 40 per cent, medical mortality, 45 per cent, and surgical mortality, 44 per cent. In Mathews' series, the total mortality rate was 16.2 per

cent, surgical mortality rate, 40 per cent; in Beretervide's series, the total mortality rate was 42 per cent.

Many authors speak of a spontaneous cure often occurring among those patients with lung abscesses. This, however, is not substantiated in this statistical group, since there was only one cured patient, and the mortality rate was 40.6 per cent, although many of these patients had been seen within the first three days of their illness and had been treated by some conservative or surgical method.

The treatment rendered these patients was primarily symptomatic. There were 3 (4.7 per cent of the total) subjected to surgery. Of these 3, 1 improved, 1 was unimproved, and 1 died. The type of treatment used in the one with improvement was rib resection with drainage of empyema resulting from the abscess. The one with no improvement had three insertions of catheter; the patient who died had thoracocentesis.

Sulfanilamide was used in 8 cases (12.4 per cent of the entire group), of which 5 patients died (62.4 per cent) and 3 (37.6 per cent) improved. Pneumothorax was attempted with one patient without improvement.

Indeed, opinion as to method of treatment which should be used varies greatly. Smith suggests that the general supportive measures, such as rest in bed, forcing of fluids, high vitamin diet, and postural drainage can be equally well applied to all types of pulmonary abscess. He believes that bacterial abscess of the gas gangrene group should be treated with specific or polyvalent antigangrene serums, that the acute staphylococcic abscesses might be treated with new staphylococcus anti-toxin, that abscesses due to other bacteria should be treated palliatively in the acute stage unless empyema develops, and that if the lesion persists for three months, it has reached the chronic stage and should be treated by open operation and drainage. The fusospirochetal type should be diagnosed and arsenic treatment started within the first two weeks if the best results are to be obtained. The mycotic abscesses of the lung should be treated by gradually increasing doses of potassium iodide.

Graham's opinion is that treatment should consist in eradication of the source of the infection, the establishment of improvement of drainage, the collapse of any cavities that may be present, the removal of chronically diseased tissue, and general hygienic treatment, including treatment with light.

Mathews made a few generalizations regarding treatment. He is of the opinion that during the acute stage lung abscesses should be handled essentially as cases of lobar pneumonia. In the case of a fusospirochetal infection or a fungus, a "suitable specific form of treatment" such as arsphenamine or the iodides might be brought into play. When a definite diagnosis of pulmonary suppuration is made, and when the child's condition can stand it, daily postural drainage should be instituted; after a few weeks if drainage is not adequate, drainage either through the bronchoscope or by thoracotomy should follow.

CONCLUSION

Mortality rate is high in the statistical report herein presented (40.6 per cent), and in all the papers surveyed (with the sole exception of Neuhof, who claims the low mortality rate of 4.5 per cent); hence it can be reasonably assumed that palliative form of therapy is inadequate and cannot restore normal lung physiology.

In review of the pathology in lung abscesses it is found that we are dealing with a rigid cavity, with tissues fixed to bony wall through adhesions, bronchi

whose muscular wall has been replaced by fibrous tissues—all of which result in a rigid fibrous mass about the abscess. Bearing these conditions in mind, extirpation of the diseased tissue seems a more feasible form of therapy.

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Announcement

In compliance with the directives imposed by the War Production Board limiting the amount of paper consumed in the production of this JOURNAL, the publishers find it necessary to change the format. As soon as these restrictions are lifted the original format will be restored. Even though the number of pages has been reduced, the actual content of the JOURNAL has not been decreased to any appreciable extent.